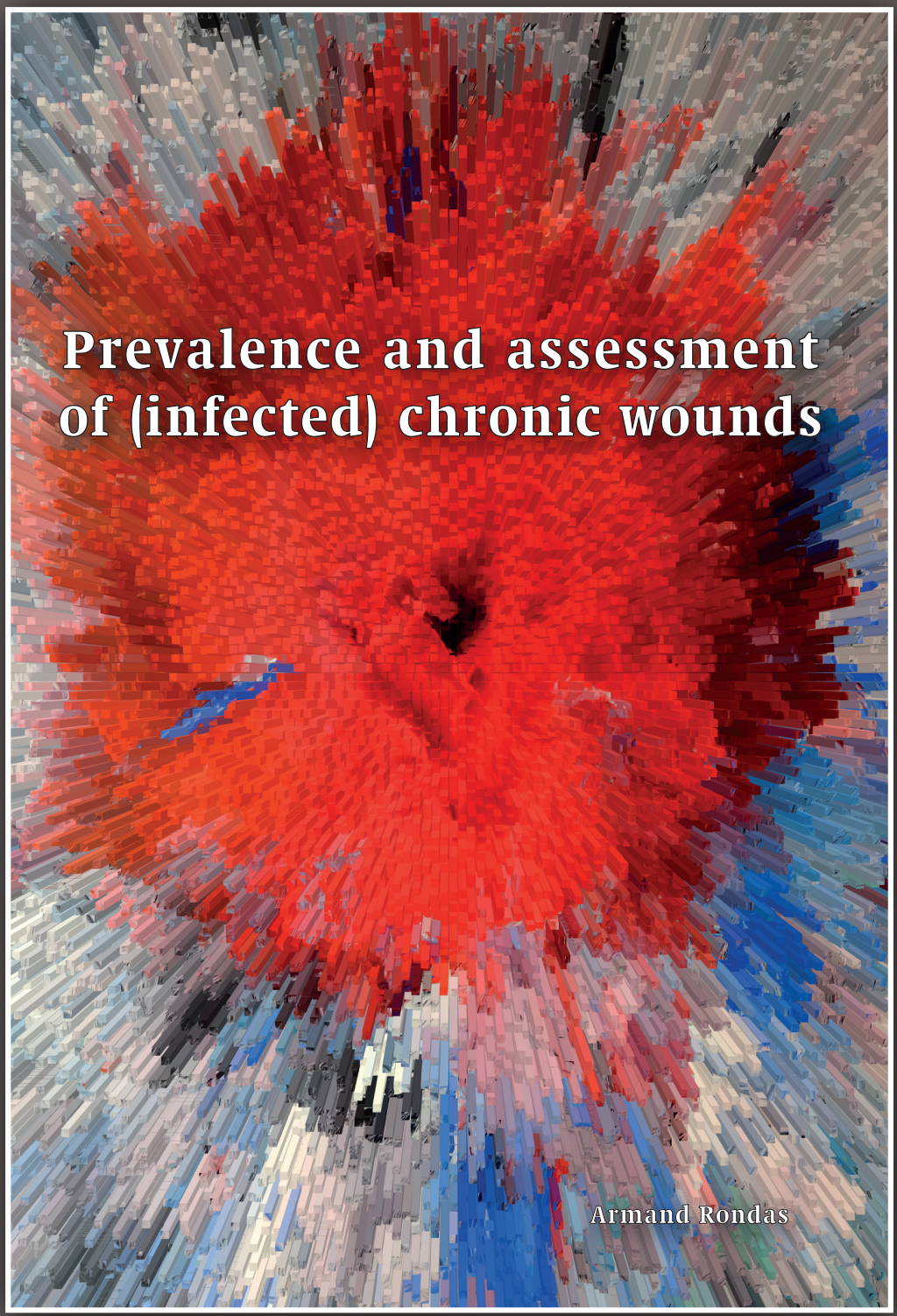
Prevalence and assessment of (infected) chronic wounds
Armand Rondas

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This thesis is dedicated to my father, Willy Rondas

Contents

Chapter 1

General introduction

General introduction

A wound can be defined as a break in the continuity of the skin. Wound healing normally occurs in a predictable sequence (coagulation, inflammation, proliferation, remodelling) and is often taken for granted. When the anatomic and functional integrity of the skin is not reached within 3 weeks, a wound is considered chronic or hard-to-heal.[1-3] Chronic wounds represent a huge challenge that inflicts a considerable encumbrance on patients, society and health care providers and thus poses a major threat to public health and the global economies[4] In developed countries, it has been estimated that 1 to 2% of the population will experience a chronic wound during their lifetime. The National Health Service in the United Kingdom has estimated the costs of chronic wounds to be €38–59 per inhabitant (€2.34–3.51 billion in total) per year.[5] In the United States, chronic wounds caused by pressure, venous stasis or diabetes mellitus affect 6.5 million patients (2% of the total population) each year and are estimated to cost in excess of €61 per year per resident (€19 billion in total).[6,7]

Patients experience chronic wounds often as painful and debilitating, resulting in the perception of a greatly reduced quality of life.[8,9] For the coming years it is expected that both the number of older patients with vascular problems and also the number of obese and diabetic patients will raise and consequently will lead to a higher incidence and prevalence of chronic wounds like arterial and venous leg ulcers, diabetic foot ulcers and pressure ulcers.

The impact on the quality of life of patients suffering from a chronic wound has been well documented.[10,11] But little is known about the prevalence of such wounds. In an urban population of London (UK), Moffat et al. identified a crude ascertainment of 0.45/1000 population (113/252000) for leg ulceration, with more than 4 weeks duration, with a mean age of 75 (range 31-94 years).[12] Except for the study of Moffat et al. there are no other studies on the prevalence of chronic wounds. Up until now no data have been published on the prevalence of chronic wounds in the Netherlands as well and more particular in specific health care settings like Dutch nursing homes.[13]

Quantifying the problem of chronic wounds, however, is an important step in improving the understanding of how chronic wounds manifest amongst people of different age groups and clinical conditions and of different health care settings. Prevalence data about chronic wounds and data about the quality of care for patients suffering from chronic wounds, may provide awareness among health care providers, managers, policymakers and politicians, and ensure a continued focus. Subsequently, interventions to improve the care for patients with chronic wounds can be initiated.

To perform successful wound care, a holistic approach is necessary with appropriate attention to the wound's underlying pathology.[14] Correcting underlying wound pathology and comorbidities is a central feature of chronic wound management.[15,16] Both systemic (i.e. diabetes mellitus and obesity, age over 60, decreased perfusion, peripheral vascular disease, malignancy, organ failure, sepsis, and restrictions in mobility) as well as local factors (wound duration, size and depth, and the presence of necrotic tissue in the wound bed) determine the rate and the extent to which wound healing takes place.[14]

Infection of chronic wounds

There is a close relationship between infection, vascular insufficiency and inflammation, because all three of them have a detrimental effect on wound healing.[14,17] Wound infection is a result of a multiplication of pathogenic micro-organisms, and results in prolonged (and excessive) inflammatory response, a delay in the synthesis of collagen, and retarded epithelialisation, as a result of microbial expression of virulence factors which ultimately results in tissue damage.[18-21]

It is highly likely that acute wounds that demonstrate the classical signs of inflammation as proposed by Celsus (rubor, tumor, calor and dolor) are infected. The definition of infection of acute wounds is based on these clinical characteristics of rapid onset and aggressive bacterial behaviour, which often respond rapidly and completely to the host immune response or prescription of antibiotics.[22,23]

The clinical assessment of chronic infected wounds is often accompanied by the identification and the assessment of the number of present isolated microorganisms. In the past, and apart from the clinical assessment, it was claimed that bacterial quantification on itself was able to assess wound infection.[24]

By itself, the quantification of more than 10^5 CFU/g (or ml) tissue wound fluid was considered as diagnostic for the presence of a wound infection.[24-28] It is known that the majority of chronic wounds are colonized with mixed microorganisms.[29] and hence simple knowledge of the wound microbiology alone may not always be helpful in the assessment of chronic wound infection.[29] For instance, the presence of *Staphylococcus aureus* in a chronic wound, as a recognized pathogenic potential, does not necessarily indicate the existence of a wound infection.[29-31]

The thinking about the significance of the microbiological load of a chronic wound has been changed in the meantime, associating a greater diversity and the potential of quorum sensing with a greater virulence and persistence of micro-organisms.[28,32-35] It also has been argued that up to 90% of all chronic wounds contains a biofilm.[36,37]

The definition of a biofilm is a community of microorganisms, either evident as mono-species or mixed species of microorganisms, attached to a surface or each other, encased within a matrix of extracellular polymeric substances (EPS) and internally regulated by the inherent population *(Figure 1)*.[38-39] Although a tissue biopsy is still considered as the gold standard for quantitative culturing [40-43] wound swabs are considered more practical and less time-consuming in their analysis.[41,44-47] However, the lack of information regarding the optimal method of collecting samples via swabbing in many studies and also the differences in wound preparation, areas sampled and transport time to the laboratory, have resulted in poor interpretation of research findings and diagnostic validity.[23,38]

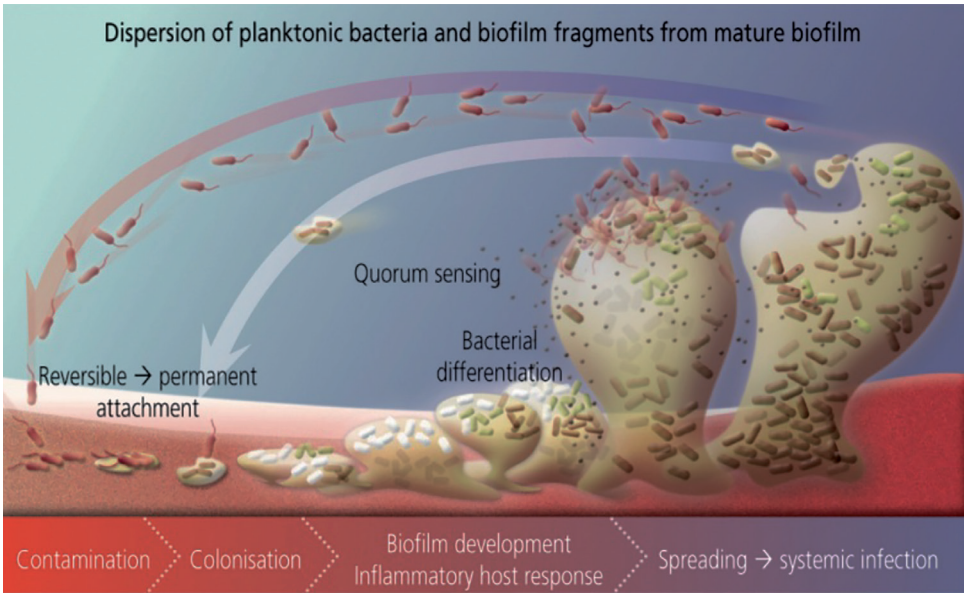

Figure 1: A diagrammatic representation of biofilm formation in a wound and the potential roles of bacterial interactions. Co-aggregation contributes to sequential binding and colonization. Bacterial interactions include metabolic communication and genetic exchange. The development of a biofilm having a high bacterial cell density increases the concentration of signalling molecules. Wound biofilms function as a barrier against deleterious factors such as antibiotics and oxygen.[39]

In this thesis we undertook two lines of inquiry. First we conducted a literature review addressing the following **research question**:

Is a wound swab using the Z- or the Levine technique, in comparison to a wound biopsy, a valid and reliable method for the diagnosis of a chronic wound infection?

Next, we executed an empirical study with **two aims**:

First:
To compare the clinical assessments of infected chronic wounds with the microbiological results of cultures taken by a swab.

Secondly:
Due to the growing number of people suffering from diabetes mellitus and peripheral arterial disease (PAD):

To compare clinician assessments with swab results of chronic wounds of patients suffering from diabetes mellitus or PAD.

Clinical assessment of infected chronic wounds

Consensus on the presence of reliable and relevant indicators to differentiate between an infected and a non-infected chronic wound is essential for efficient management and careful antimicrobial treatment of these wounds, as well as for reducing negative economic, health and care consequences.[49] However, the clinical assessment of a chronic wound infection is challenging. In contrast to the overt signs and symptoms of acute wounds, the signs and symptoms of chronic wounds are subtle, and therefore more difficult to interpret.[23,50,51] In 1994 Cutting and Harding proposed the use of additional infection criteria as apposed to relying solely on the 'traditional' signs such as abscess, cellulitis and discharge (i.e. the classic inflammatory signs; rubor, dolor, calor and tumor).

These additional criteria may be applied to a variety of open granulating wounds as a result of surgery, healing by secondary intention. But not to burns or leg ulcers, as they have not been tested in these situations.[52] In order to explore the subtle signs and symptoms associated with the identification of infection in specific wound types, Cutting et al. recruited an international multidisciplinary Delphi expert group of 54 members in 2005. Criteria were grouped into three categories according to their scores: 4-5 (important), 6-7 (very important), 8-9 (diagnostic). The structure of the categories was driven by the data.[50] Criteria consistently ranked as 8-9 were considered to be diagnostic of infection, whereas criteria achieving lower scores (6-7 or 4-5) were perceived as more subtle clinical indicators or signposts of infection.

In 2008, an international consensus document on wound infection in clinical practice was published by the World Union of Wound Healing Societies.[23] Several sets of signs and symptoms were suggested for the assessment of wound infection of both acute and chronic wounds, which were based on published literature and expert opinion *(Table 1)*.

Table 1: Signs and symptoms of acute and chronic wound infection according to the consensus document of the WUWHS on wound infection.[23]
*individually highly indicative of infection. Infection is also likely in the presence of two or more of the other signs listed.

Signs & symptoms of acute wounds	Signs & symptoms of chronic wounds
Classical signs and symptoms: • new or increased pain • erythema • local warmth • swelling • purulent discharge	Delayed healing*
	Pain/more pain*
	New pain*
	Redness
	Heat
	Edema
Pyrexia	Induration
Delayed or stalled healing	Odour
Abscess	Wound exudate
Malodour	Discolouration of granulation tissue
Further extension of erythema	Pocketing of the wound base
Lymphangitis	Bridging
Crepitus in soft tissue	Crepitation
Wound breakdown/dehiscence	Lymphangitis

Despite these advances, assessing chronic wound infection and the prescribing of antibiotic treatment remains challenging. Antibiotics are often prescribed prematurely, as a precaution to avoid a potential life threatening deterioration of the patient and his wound.[53] This is not surprising because the indication for antibiotics along with the optimal treatment strategy has not yet been clearly defined.[14,49,54] The chronic wound patient population is of vital importance due to; the high use of antibiotics, the associated microbiological load of the wounds and the risk that chronic wounds pose for the spreading of resistance.[49] The precise contribution to the overall development, maintenance and dissemination of resistance as a result of antibiotic prescriptions for the treatment of chronic wounds is not yet known.

Chronic wounds in Dutch nursing homes

In 2010 the maximum capacity of Dutch nursing homes and elderly homes was 158,000, of which 78,000 beds were available in nursing homes.[55] Nursing homes in the Netherlands offer care for both physically frail as well as demented residents. Their clinical profile is characterized by considerable comorbidities next to the main diagnosis, polypharmacy and a high level of care dependency. To offer these residents adequate multidisciplinary care, nursing homes employ their own multidisciplinary staffs, consisting of elderly care physicians, nurses, physiotherapists, occupational therapists, speech therapists, dieticians, psychologists, social workers, pastoral workers, and recreational therapists.[56]

Because nursing home residents next to their high age show a clinical profile of multiple morbidity it can be expected that (infected) chronic wounds also show a high prevalence in this target group. Despite that no data have been published on the prevalence of chronic wounds and wound care policy related to chronic wounds in Dutch nursing homes.[13] Therefore we performed a first explorative study, with the following **research questions**:

What is the number of chronic pressure ulcers (PUs), chronic post-traumatic wounds, chronic venous leg ulcers (VLUs), and chronic arterial ulcers and diabetic ulcers in Dutch nursing homes, as treated by Dutch nursing home physicians (NHPs)?

How many of the chronic wounds treated, do NHPs consider to be infected?

How do the top five clinical signs and/or symptoms of infection for different types of chronic wounds as ranked by Dutch NHPs compare with the rankings made by an international multidisciplinary Delphi group in 2005? [50]

Subsequently this explorative study prompted us to conduct further research and to measure the prevalence of (infected) chronic wounds and quality of care delivered in Dutch nursing homes more in depth.

Prevalence of (infected) chronic wounds in Dutch nursing homes

Since 1998 the Dutch National Prevalence Measurement of Care Problems (LPZ) annually measures the prevalence and associated quality indicators of different healthcare problems in Dutch nursing homes, amongst which pressure ulcers, incontinence, malnutrition and falls.[57-59] For this PhD project, in 2012 the LPZ was expanded with the Module 'Chronic wound' and for the first time it was possible to measure the prevalence of (infected) chronic wounds and related quality indicators in Dutch nursing homes more in detail.
Using this module, we performed a study with the following **research questions:**

What is the prevalence of (infected) chronic wounds in Dutch nursing homes?

What are the most common types of chronic wounds, wound locations on body and actual duration of these wounds?

Which signs and symptoms are used to diagnose infected chronic wounds?

Which dressings are used for the management of chronic wounds?

Which structural quality indicators related to chronic wounds at ward and institutional level are fulfilled in Dutch nursing homes?

How to obtain high quality and cost effective wound care in patients with chronic wounds?

It is paramount that clinical practitioners have a thorough understanding of current diagnostic modalities and principles of chronic wound care in an effort to improve patient outcome and reduce costs. But similar to the situation in the 90s in the UK[60], the treatment of chronic wounds in the Netherlands is still rather fragmented, ineffective and lacking adequate professional standardisation. Patients receive treatment in a scattered landscape of intra- and extramural working health care professionals, such as family doctors, medical specialists, and elderly care specialists, physician assistants, nursing specialists, district nurses, paramedics, occupational therapists, podiatrists and dieticians.

Therefore, in 2011, van Mierlo-van den Broek recommended an innovative organization of chronic wound care in the Netherlands. The main elements of this innovative way of organizing wound care involved the possibility of a quick referral of a patient with a chronic wound to a genuine wound care specialist team/wound care centre in which a comprehensive multidisciplinary wound assessment is performed, followed by a strictly monitored and targeted intervention.[3]

In succession of several cost effective examples of community based leg ulcer clinics in the UK at the end of last century [61-64] an outpatient wound clinic, the Knowledge Centre in Wound Care (KCWC) was founded in Venray, the Netherlands in 2009. The KCWC accepts all kinds of chronic wounds. Patients are mostly referred by their general practitioner (GP). During intake, patients are seen by one of the nurses together with the specialized wound clinic physician. Evaluating each patient's wound leads to an underlying diagnosis and is followed by formulating a multidisciplinary tailor-made wound treatment plan.

Other specialists such as a podiatrist, occupational therapist or orthopaedic shoemaker may be involved in the patients' treatment plan. The patients follow-up is conducted during regular consultations at the wound clinic in collaboration with home care nurses who strictly execute the wound treatment plan at home. Although the phenomenon of an outpatient wound clinic meets the substantive argument for an innovative organization of chronic wound care in the Netherlands. It is not clear whether such an approach is cost-effective. Therefore we conducted an economic evaluation of the KCWC with the **research question**:

From an insurance perspective, is there a difference in healthcare costs (specifically, costs that qualify for reimbursement under the Health Insurance Act) in the year before a patient's first visit to the KCWC and the year following a patient's first visit to the KCWC?

Outline of the thesis

Chapter 2 presents the study involving the explorative survey in Dutch nursing homes.

Chapter 3 presents the larger study on the prevalence and related quality indicators of chronic (infected) wounds in Dutch nursing homes.

Chapter 4 describes the results of the literature review to answer the research question whether a swab using the Z- or Levine technique, as compared to a biopsy, is a valid and reliable method for the assessment of an infection of a chronic wound.

Chapter 5 presents the results of the study conducted at the outpatient wound clinic in Venray, to explore whether a qualitative and/or semi-quantitative assessment done after swab taking is supportive to the clinical assessment of a wound infection, making use of the 13 signs and symptoms of chronic wound infection, mentioned in the international consensus document on wound infection of the WUWHS. From each wound, a standardised wound swab was taken, using the Levine technique; subsequently all swabs were analysed microbiologically to assess the presence of an infection.

Chapter 6 provides the results of the cost analysis of one of the first outpatient community-based wound care clinics in Venray, the Netherlands. Differences in wound-related health care costs of patients are analyzed between the year before and the year after their first visit at the wound clinic.

Chapter 7 a general discussion reflects on the studies which are part of this thesis (chapter 2-6).

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Chapter 2

Definition of infection in chronic wounds by Dutch nursing home physicians

Rondas AALM, Schols JMGA, Stobberingh EE, Price PE

International Wound Journal 2009 Aug;6(4):267-74. doi:10.1111/j.1742-481X.2009.00604.x.
Erratum in: International Wound Journal 2009;6(5):404

Abstract

Aims of the study

This study investigated the number and types of chronic wounds treated by Dutch nursing home physicians (NHPs). The study also aimed to identify how many of the treated chronic wounds the NHPs considered infected. The NHPs were asked to select and rank their top five criteria for chronic wound infection from a list provided. The ranking was then compared with the selections made by an international multidisciplinary Delphi group of wound experts in 2005.

Method

A cross-sectional descriptive survey was conducted using the information from a self-reported questionnaire that was filled in by a representative sample of Dutch NHPs. In total, 361 NHPs (25%) were sent a questionnaire. Of these, 139 NHPs (38.5%) filled in and returned the questionnaire, of which121 were valid to be used in the analyses.

Results

At the time of the survey, 73.5% of the responding NHPs was treating at least one chronic pressure ulcer (PU), and 26.5% was treating none. Of the NHPs, 31.6% was treating at least one, but never more than two, chronic post-surgical wounds, while 68.4% was treating none. Chronic venous leg ulcers (VLUs), arterial ulcers and diabetic ulcers were being treated less frequently than the other two types of chronic wounds. Of the PUs, 53% were considered to be infected. The other chronic wounds were considered to be infected far less frequently. Dutch NHPs appeared to use more 'traditional' criteria such as 'puss/abscess' and 'malodour' to identify infection.

Conclusions

According to this study, NHPs do not frequently treat chronic wounds. PUs are treated most frequently. For NHPs, identifying infection in all types of chronic wounds is difficult. The use of unreliable criteria for diagnosing chronic wound infection may lead to ineffective treatment and can even cause serious harm to patients. Nevertheless, the clinical identification of infection still depends primarily on expert opinions. Both research on triggers for suspicion of infection of chronic wounds and the development of evidence-based guidelines for the identification of infected chronic wounds are needed.

Key words: chronic wounds, wound infection, clinical criteria, nursing home, Dutch nursing home physicians.

Introduction

Wound healing can be defined as the process of tissue repair involving the tissue response to injury.[1] The normal wound healing process can be divided into a series of artificially defined events. It starts with haemostasis and then involves an inflammatory response, the formation of connective tissue, the covering of the wound with epithelium, and the remodelling of the wound. These different phases normally proceed without difficulty, and uncomplicated small wounds are expected to heal and reepithelialise within a period of three weeks.[1]

However, the normal process of wound healing can be fraught with problems and altered at many points. Both intrinsic and extrinsic factors may contribute to wound recalcitrance. Determining these factors is essential in formulating a successful treatment plan.[2] Although an accurate history may help to determine the initial aetiology of the wound, the chronicity of dermal wound healing seems more related to secondary factors, such as infection or vascular insufficiency.[3] Chronic wounds affect more than 1% of the UK population and cost British society at least £1 billion per year.[4] The costs, both financially and emotionally, are indisputably high.

In Dutch nursing homes, approximately 44,000 new patients are admitted each year. In general, these are very frail and disabled elderly people at an average age of 80, who often have considerable care dependency, (co)morbidity and frequent disabilities.[5,6]

Since 1968, the Dutch nursing home has evolved from a place for discharged hospital patients to receive chronic care nursing to a facility where nursing is integrated with continuing paramedical and medical care. Patients are supported in reaching an optimal level of functioning. Since 1989, 'nursing home medicine' (nowadays called elderly care medicine) has been an officially recognised medical discipline in the Netherlands, which is unique in the world.[6,7]

Chronic wounds tend to occur as a result of poor local factors (arterial insufficiency, venous hypertension and trauma) and/or the presence of a systemic disease such as diabetes mellitus or rheumatoid arthritis.[8] Wound infection interferes with normal wound healing and occurs when microbes invade viable tissue. This causes a prolonged and excessive inflammatory response, delays collagen synthesis, retards epithelialisation and creates more tissue damage.[8-12] If wound infection is allowed to progress naturally, local infection may place the patient at risk for systemic complications, sepsis and osteomyelitis, and might even lead to death. Wound infection and its associated delayed healing present a considerable challenge for clinicians with regard to the clinical identification of infection and the choice of appropriate treatment. Pain, erythema, edema and warmth are known as 'classical' signs of inflammation. In contrast to the often overt signs and symptoms of infection in acute wounds, in chronic wounds these signs and symptoms may be quite subtle.[13]

For quantifying bacteria in wounds, quantitative tissue biopsies or swab samples can be used. Research by Bendy et al. and Robson et al. formed the basis of the '10^5 guideline' in wound care,[14-17] which has become disputed as an indicator of chronic wound infection.[18,19] The number of microorganisms seems less significant than the presence of particular species that have the potential of quorum sensing to improve their virulence and persistence.[10,18,19]

In order to explore the more subtle signs and symptoms associated with identifying infection in chronic wounds, Cutting et al. (2005) recruited an international multidisciplinary Delphi group of 54 members. Group members, allocated to one of six panels related to their individual areas of expertise, were asked to list the clinical indicators of infection relevant to one wound type. Criteria were grouped into three categories according to their scores: 4-5 (important), 6-7 (very important), 8-9 (diagnostic). The structure of the categories was driven by the data.[20] This study applies the work of the Delphi group to the nursing home sector in the Netherlands. This article focuses on wounds that have become chronic as a result of infection, with special reference to their occurrence and assessment in the nursing home setting in the Netherlands.

The following questions are addressed:

- What is the number of chronic pressure ulcers (PUs), chronic post-traumatic wounds, chronic venous leg ulcers (VLUs), and chronic arterial ulcers and diabetic ulcers in Dutch nursing homes, as treated by Dutch nursing home physicians (NHPs*)?
- How many of the chronic wounds treated, do NHPs consider to be infected?
- How do the top five clinical signs and/or symptoms of infection for different types of chronic wounds as ranked by Dutch NHPs compare with the rankings made by an international multidisciplinary Delphi group in 2005 (EWMA 2005)?[20]

* Since 2009 the NHP is officially called elderly care physician (in this article the abbreviation NHP is still used).

Methods

A cross-sectional descriptive survey was conducted using the information from self-reported questionnaires in a representative sample of all 1,433 Dutch NHPs, taken from the list of the Dutch Association of Nursing Home Physicians (NVVA at Utrecht, the Netherlands: now called Verenso: www.verenso.nl). Every *fifth* record from the list of Dutch Association members was taken systematically. Between December 2006 and March 2007, the 361 sampled NHPs (25%) were sent the questionnaire together with an accompanying explanatory letter. The questionnaire was designed to collect quantitative and qualitative information. The NHPs were asked to indicate the numbers of chronic PUs, chronic post-surgical wounds, chronic VLUs, chronic arterial ulcers and chronic diabetic ulcers they were currently treating.

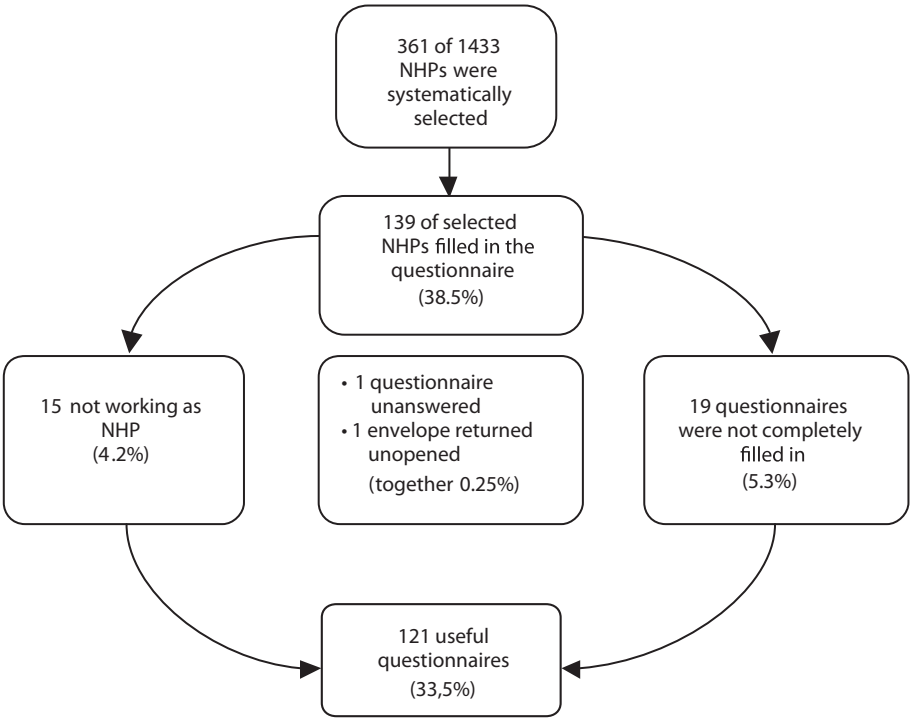
The other questions addressed the NHPs' knowledge in diagnosing chronic wound infection. The NHPs were asked to consider the clinical symptoms of chronic wound infection and to select their five most significant signs and symptoms per chronic wound type from a list provided. The signs and symptoms on the provided list were the same as those indicated by the European Wound Management Association's position document.[20]

As patients did not participate, there was no need for ethical approval or permission from a Medical Ethics Committee under the ethical framework used in the Netherlands. However, the anonymity and privacy of participants was respected and kept confidential and secure. The data from the questionnaire were processed using SPSS13 for Windows, 2004 (SPSS Inc, Chicago, IL, USA).

Results

Of the 361 NHPs who were sent the questionnaire, 139 (38.5%) filled it in and returned it. In addition, 15 were excluded because they were not working as an NHP. One envelope was returned unopened and one respondent returned the questionnaire unanswered; 19 of the returned questionnaires were not filled in completely. Ultimately, 121 (33.5% of total sample) of the returned questionnaires could be used for this study *(Fig. 1)*. Of these respondents, 66% was female and 34% male. Of the non-respondents, 61% were female and 39% male. Of all Dutch NHPs in 2005 (1,177), 58% was female and 42% male.[21] The answered questionnaires were returned in equal numbers from all the provinces of The Netherlands.

Figure 1. Flow diagram of nursing home physicians who responded to the questionnaire.



Chronic PUs

Of the Dutch NHPs, 73.5% was treating at least one chronic PU at the time of the survey, while 26.5% was treating none *(Table 1)*; 53% considered none of these chronic PUs to be infected *(Table 2)*.

Table 1. Types and frequencies of chronic wounds treated by Dutch nursing home physicians.

Number of patients with chronic wounds	Pressure ulcers %	Post-surgical wounds %	Venous leg ulcers %	Arterial ulcers %	Diabetic ulcers %
0	26.5	68.4	76.9	82.9	80.2
1	20.5	21.3	20.5	16.2	14.7
2	19.7	10.3	2.6	0.8	4.3
3	16.2	-	-	-	0.9
4	10.3	-	-	-	-
5	0.8	-	-	-	-
>5	6.0	-	-	-	-

Chronic post-surgical wounds

Of the Dutch NHPs, 31.6% was treating at least one but not more than two chronic post-surgical wounds, while 68.4% of the NHPs was treating none (Table 1); 12% considered one of the chronic post-surgical wounds to be infected, and 83.8% considered none of these wounds to be infected *(Table 2)*.

Table 2. Percentages of chronic wounds diagnosed as infected.

Number of patients with chronic wounds	Pressure ulcers %	Post-surgical wounds %	Venous leg ulcers %	Arterial ulcers %	Diabetic ulcers %
0	53	83.8	88.1	90.5	91.4
1	27.4	12	11.1	8.6	6.8
2	11.1	4.2	0.8	0.9	0.9
3	4.3	-	-	-	0.9
4	3.4	-	-	-	-
5	0.8	-	-	-	-
>5	-	-	-	-	-

Chronic VLUs

Of the Dutch NHPs, 23.1% was treating at least one but not more than two chronic VLUs, and 76.9% was treating none (Table 1); 88.1% considered none of these chronic VLUs to be infected *(Table 2)*.

Chronic arterial ulcers

Of the Dutch NHPs, 17% was treating at least one but not more than two chronic arterial ulcers *(Table 1)*, and 90.5% considered none of these arterial ulcers to be infected *(Table 2)*.

Chronic diabetic ulcers
Of the Dutch NHPs, 19.9% was treating at least one but not more than three chronic diabetic ulcers, and 80.2% was treating none *(Table 1.)*; 91.4% considered none of the chronic diabetic ulcers to be infected *(Table 2)*.

II. Qualitative assessment of signs and/or symptoms of chronic wound infection

The 121 Dutch NHPs selected their top five signs and/or symptoms of infection for the different chronic wound types from a list consisting of twenty-five symptoms that had been discussed by Cutting et al *(Table 3)*.[20] In *Table 3*, the ranking of these signs and/or symptoms by NHPs is indicated, using colours. Different symptoms that were selected at the same frequency are shown as having the same ranking.

Table 3. The five most important signs and symptoms of infection by wound type.

Signs and symptoms Delphi criteria	Pressure ulcers	Post-surgical wounds	Venous leg ulcers	Arterial ulcers	Diabetic ulcers
Cellulitis					
Malodour	18.8 %	14.4 %		13.2 %	14.0 %
	16.5 %				14.2 %
	12.4 %			14.4 %	13.2 %
Change in nature of pain		12.0 %			
Delayed healing		11.9 %	9.9 %		14.2 %
Deterioration of the wound/wound breakdown	12.2 %				
Erythema		11.9 %			
Pus/abscess	44.4 %	51.8 %	32.4 %	36.5 %	34.4 %
		16.8 %	12.6 %	15.0 %	19.6 %
Lymphangitis					
Crepitus					
Increase in exudate volume					
Necrosis – new or spreading					
Base changes from healthy pink to yellow or grey					
Sudden increase in size			11.6 %		
Oedema					
Fluctuation					
Wound stops healing despite measures		11.9 %			
B Bone or tendon becomes exposed at base					
Induration					
Pocketing					
Viable tissue becomes sloughy					
Dry necrosis turning wet					
Increase on local skin temperature			9.9 %	13.3 %	
			10.7 %		
Change in wound bed colour					
Friable granulation tissue that bleeds easily					
Probes to bone					

Ranking of five most important signs & symptoms	Colour
1	
2	
3	
4	
5	

Chronic PUs

Of the NHPs, 44.4% judged 'pus/abscess' as the number one symptom that caused them to suspect wound infection, and 18.8%, 16.5% and 12.4% of the NHPs ranked 'malodour' in either position two, three or five. 'Deterioration of the wound/wound breakdown' was number four in the ranking because 12.2% of the NHPs chose this sign *(Table 3)*. Four NHPs failed to rank the first two signs and/or symptoms, and six did not rank the third and fourth most important symptoms. Eight NHPs did not select their 'least important' symptom.

Chronic post-surgical wounds

The NHPs regarded 'pus/abscess' as the most significant sign/symptom of infection: 51.8% chose it as number one and 16.8% set it at number two; 'malodour' was equally ranked as 'wound stops healing despite measures', chosen by respectively 14.4% and 11.9% as third sign/symptom. 'Erythema' and 'delayed healing' were both chosen by 11.9% as the fourth symptom; and 'change in nature of pain' was set as the fifth symptom by 12.0% of the NHPs *(Table 3)*. Respectively, 9, 8, 10, 12, and 13 of the NHPs did not rank each of the five most important symptoms.

Chronic VLUs

Of the NHPs, 32.4% considered 'pus/abscess' as the most important symptom for identifying infection of a chronic VLU, and an additional 12.6% ranked 'pus/abscess' as the second symptom. 'Increase in local skin temperature' and 'delayed/arrested wound healing despite measures' were both chosen equally; 9.9% ranked 'increase in local skin temperature' and 'delayed/arrested wound healing despite measures' as third most important symptoms. Of the NHPs, 10.7% chose 'increase in local skin temperature' as number four, and 11.6% chose 'sudden increase in size' as number five *(Table 3)*. Ten NHPs did not fill in their top three symptoms; 11 and 12 of the NHPs did not rank symptoms four and five, respectively.

Chronic arterial ulcers

'Pus/abscess' was considered as the most important symptom by 36.5% of the Dutch NHPs for identifying the presence of infection and was also chosen as the second symptom by 15% of the NHPs. 'Malodour' was ranked as the third and fifth symptoms by 13.2% and 14.4% of the NHPs, respectively. 'Increase of local skin temperature' was chosen by 13.3% as the fourth most important symptom *(Table 3)*. The first and second most important symptoms were not filled in by 14 NHPs; the third not by 15 respondents; the fourth not by 16 NHPs and 17 did not rank the fifth symptom.

Chronic diabetic ulcers

Of the NHPs, 34.4% considered 'pus/abscess' as the most significant symptom for indicating infection, and 19.6% chose 'pus/abscess' as their number two. 'Malodour' was ranked third, fourth and fifth by 14.0%, 14.2% and 13.2%, respectively. 'Delayed/arrested wound healing despite measures' was also ranked third by 14.2% of the NHPs *(Table 3)*.

III. Do the selected criteria for chronic wound infection match with those of Cutting et al.?

Chronic PUs
The rankings of the sample of Dutch NHPs did not match with the criteria of Cutting et al. Unlike Cutting et al., the Dutch NHPs considered 'pus/abscess' and 'malodour' to be important indicators of chronic pressure ulcer infection.[20]

Chronic post-surgical wounds
The selections of the Dutch NHPs matched with the criteria of Cutting et al.[20] The NHPs' ranking of 'pus/abscess' corresponds with the ranking of the experts of the Delphi group. The Delphi experts also mentioned 'cellulitis' as a significant symptom of infection. 'Malodour' and 'erythema' scored less in both groups and seemed mutually comparable between the NHPs and the Delphi panel experts.

Chronic VLUs
The ranking of the Dutch NHPs did not match with the criteria of Cutting et al.[20] Unlike the Delphi experts, the Dutch NHPs regarded 'pus/abscess' to be more diagnostic than 'cellulitis'. For both the Dutch NHPs and the Delphi experts, the symptoms 'delayed/ arrested wound healing despite measures' and 'increase in local skin temperature' had only additional value in the diagnosis of chronic VLU infection.

Chronic arterial ulcers
For Cutting et al., both the symptoms 'pus/abscess' and 'cellulitis' were equally important in the suspicion of infection of a chronic arterial ulcer. The NHPs considered 'pus/abscess' to be far more important and did not mention 'cellulitis' in the ranking. The NHPs scored 'malodour' higher than the Delphi experts scored it.

Chronic diabetic ulcers
The NHPs chose both 'pus/abscess' and 'malodour' as the most important symptoms. Besides 'pus/abscess', the Delphi experts also gave 'cellulitis', 'lymphangitis', 'phlegmon' and 'purulent exudate' a high rank. Unlike the Dutch NHPs, the Delphi experts considered 'malodour' less important.

Discussion

Considering the intake of 44,000 patients in Dutch nursing homes each year, it is striking that no scientific literature is available about chronic wounds and infection of chronic wounds in this patient group. This study gives an indication of the number of chronic PUs, chronic post-traumatic wounds, chronic VLUs, chronic arterial ulcers and chronic diabetic ulcers as treated by Dutch nursing home physicians.With the exception of PUs, the prevalence of other chronic wounds in the Netherlands is unknown. Since 1998, the prevalence of PUs has been measured in nursing homes by the Dutch National Prevalence Measurement of Care Problems (LPZ). In 2008, more than one-third (119) of Dutch nursing homes participated. The LPZ determined the prevalence of PUs to be 6.1% (that is without grade I) in Dutch nursing homes in 2008, and the results of this study match those of the LPZ.[22]

In the Netherlands, approximately 26,000 hip prostheses and nearly 19,000 knee prostheses are completed each year. In 2007, 5,400 orthopaedic patients were transferred from Dutch hospitals to nursing homes for rehabilitation.[6,23] The small number of chronic post-surgical wounds indicated in this study, seems to be in contradiction to the substantial number of patients who go through a long-term rehabilitation program in Dutch nursing homes. From a health district in the United Kingdom and from a metropolitan population in Perth, Western Australia, a prevalence of 1.48-3.3/1,000 patients for chronic VLUs can be derived.[24-26] Given the specificity of the population of frail and disabled elderly in Dutch nursing homes, it may be expected that Dutch NHPs should treat chronic VLUs more often than is indicated in this study.

The prevalence of diabetes mellitus in the Netherlands was estimated to be over 600,000 patients in 2003, with a prevalence of 10% in people over sixty years of age.[27] Dutch NHPs and Dutch family physicians may underestimate the problem of diabetic ulcers, given that they indicate that they do not treat many of these.[28] The results of this study show a clear difference in the signs and/or symptoms used to identify infection in chronic PUs versus other types of chronic wounds. Although the cause of this difference is unknown, Dutch NHPs are professionally more focussed on PUs than on other types of wounds. The Dutch Health Care Inspectorate has declared the prevalence of PUs as a quality indicator and in 2003, in contrast to other types of wounds, set up an occupational guideline on PUs for Dutch NHPs.[29,30]

Furthermore, Dutch NHPs appear to neglect other criteria of infection in chronic wound types that were outlined by Cutting et al.[20] They also tend to hold tight to more 'traditional' criteria of wound infection, such as 'pus/abscess' and 'malodour'. It seems that the available scientific literature has not yet been implemented in wound care. Alternatively, the answers given by Cutting et al. may not be indisputably 'right' answers, and this reflects the difficulties associated with diagnosing infection in complex wounds.[20]

The international guideline of the World Union of Wound Healing Societies indicates triggers for suspecting wound infection and focuses merely on the difference between acute and chronic wounds. 'Purulent discharge' and 'malodour' are especially shown as triggers for suspecting a localised infection in an acute wound.[31]

The methodology used in this study is limited by the ambiguity of the definitions used and the term 'importance' in relation to the ranking of the NHPs. However, the results of the study may be considered to be representative of Dutch NHPs with regard to the relatively equal distribution of male and female respondents and non-respondents.

Conclusions

According to this study, NHPs do not frequently see chronic wounds. Of all types of chronic wounds, PUs are treated in the greatest numbers. For NHPs, identifying infection in all types of chronic wounds is difficult . To provide a more accurate measure of the prevalence of infected chronic wounds and infection in chronic wounds in Dutch nursing homes, further research is needed. The use of unreliable criteria for diagnosing chronic wound infection may lead to ineffective treatment and can even cause serious harm to patients. Nevertheless the clinical identification of infection still depends primarily on expert opinions. Further research on triggers for suspicion of infection of chronic wounds and also the development of evidence-based guidelines for the identification of infected chronic wounds are needed.

Conflict of interest

The authors of this article declare that there is no conflict of interest or any financial or personal relationships with other people or organisations that had an inappropriately influence (bias) on this work.

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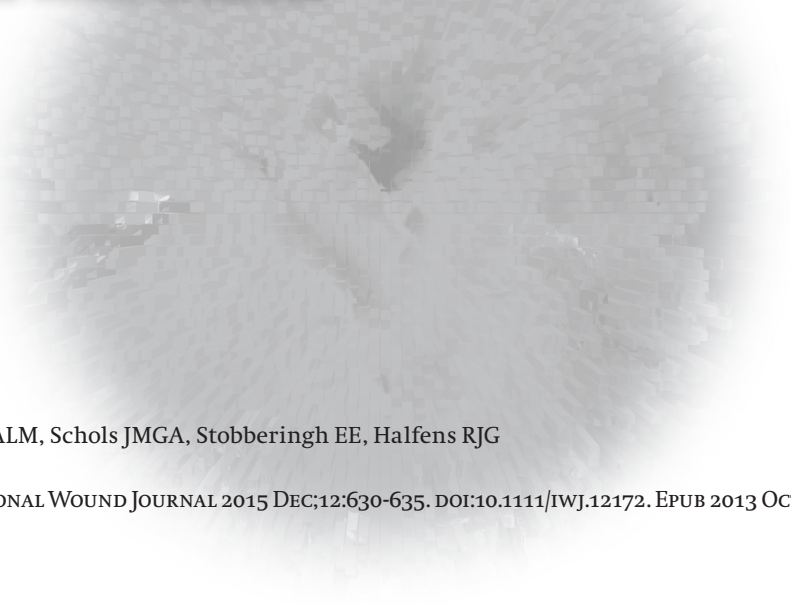
Chapter 3

Prevalence of chronic wounds and structural quality indicators of chronic wound care in Dutch nursing homes



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Abstract

Introduction

It was the aim to measure the prevalence of (infected) chronic wounds in Dutch nursing homes and to explore which signs and symptoms are used to diagnose infected chronic wounds. Moreover, it was to determine which structural quality indicators related to chronic wound care at ward and institutional level were fulfilled.

Method

In April 2012, as part of the annual National Prevalence Measurement of Care Problems of Maastricht University (LPZ), a multi-center cross-sectional point-prevalence measurement was carried out together with an assessment of relevant care quality indicators.

Results

The prevalence was 4.2%. 16 out of 72 (22%) chronic wounds were considered to be infected. Increase of exudate (81.3%; n=13), erythema (68.8% ; n=11), pain (56.3%; n=9) and wound recalcitrance (56.3%; n=9) were considered to be diagnostic signs and symptoms of a chronic wound infection. Although at institutional level most quality indicators were fulfilled, at ward level this was not the case.

Discussion

Despite the relatively low number of residents, we consider our population as representative for the nursing home population. It may be an advantage to appoint specific ward nurses and to teach them specifically on knowledge and skills concerning chronic wounds.

Key words: chronic wound, infection, prevalence, quality indicators.

Introduction

When wound healing does not proceed normally, and the anatomic and functional integrity of the skin is not reached within a few weeks, a wound is considered to be chronic.[1,2] Although a chronic wound is often just defined by mentioning the wound type based on different underlying aetiology, as pressure ulcers, venous leg ulcers, and diabetic foot, knowledge of intrinsic and extrinsic factors that contribute to wound recalcitrance is essential to perform successful wound care.[3,4] Vascular insufficiency and infection are important factors responsible for the non-healing of wounds.[5] Wound infection implies the multiplication of micro-organisms resulting in a prolonged (and excessive) inflammatory response, a delay in collagen synthesis, retarded epithelialisation and finally in tissue damage.[6,7,8,9] In 1994, Cutting and Harding reviewed the literature and demonstrated the signs and symptoms to rely the diagnosis of wound infection.[10] In 2008 the World Union of Wound Healing Societies published her guideline on diagnosing wound infection.[11]

In improving the care for patients with chronic wounds, it is important to have insight in the prevalence of chronic wounds, the characteristics of patients vulnerable for chronic wounds and the signs and symptoms of chronic wound infection. Getting attention and being aware of a problem are the first steps in the process of improving care. With prevalence data about chronic wounds and the quality of care for patients with chronic wounds, awareness can be created in caregivers, managers, policymakers and politicians. Subsequently, interventions to improve the care for patients with chronic wounds can be initiated. Since 1998 The Dutch National Prevalence Measurement of care problems (LPZ) measures yearly the prevalence and related quality indicators of different care problems including pressure ulcers, incontinence, malnutrition, falls, restraints and intertrigo. Since 2012 the LPZ focuses also on chronic wounds. This study describes the results of the first LPZ measurement of chronic (infected) wounds in Dutch nursing homes.

In the Netherlands disabled persons with physical diseases or with progressive dementia, mainly elderly that are not able to manage their daily activities, who suffer from a lot of comorbidity and care problems and who need plural, more complex continuing care are often admitted to a nursing home. There are about 345 nursing homes with in total about 63,000 beds, 27,000 in somatic wards and 36.000 in psychogeriatric wards. Nursing homes employ their own multidisciplinary staffs, consisting of elderly care physicians, nurses, physiotherapists, occupational therapists, speech therapists, dieticians, psychologists, social workers, pastoral workers, and recreational therapists.[12] Until now, no data have been published on the prevalence of chronic wounds and wound care policy related to chronic wounds in Dutch nursing homes.

The aims of this study were to answer the following questions:

- What is the prevalence of (infected) chronic wounds in Dutch nursing homes?
- What are the most common types of chronic wounds, wound locations on body and actual duration of these wounds?
- Which signs and symptoms are used to diagnose infected chronic wounds?
- Which dressings are used for the management of chronic wounds?
- Which structural quality indicators related to chronic wounds at ward and institutional level are fulfilled in Dutch nursing homes?

Method

Design

This study was part of the annual National Prevalence Measurement of care problems of Maastricht University (Landelijke Prevalentiemeting Zorgproblemen (LPZ), Van Nie et al. 2013).[13] The design of the study involved a multi-centre cross-sectional point-prevalence measurement and was carried out in April 2012.

Sample

For the LPZ study, all the 345 nursing home organisations in the Netherlands were invited by mail to participate voluntarily. Of the 158 participating elderly organisations, 21 nursing home organisations agreed to participate in the module chronic wounds. Patients were included if they gave informed consent, and were 18 years or older.

Data collection

This annual LPZ measurement took place at the 3th of April 2012. Each participating organisation appointed a coordinator, who was responsible for organising the measurement. The coordinators were trained collectively by the research group on how to manage the survey, and how to use the standardised questionnaires and the specially designed internet data-entry program (www.LPZ-UM.eu). As a regular procedure, to achieve objective judgment for every patient, all patients were assessed by a rater pair of two healthcare professionals (nurses or physicians; one of whom worked on the patient's ward and one independent). The coordinators also received a protocol and training package to support them in training the healthcare professionals who would perform the measurement within their organisations. LPZ participants could find all the information needed for the measurement and data entry on a purpose-built website. The LPZ measurement includes several care problems. Each institution can decide which care problems will be measured.

Instrument

For the care problem module chronic wounds a standardised questionnaire focusing on four levels being wound, patient, ward and nursing home, was used. On wound level, a rater pair assessed whether a patient had a wound, which lasted more than three weeks. If so, an experienced wound care nurse, or when not available, the elderly care physician (ECP), filled in a questionnaire about each chronic wound. Besides questions related to the type of the chronic wound and whether the wound was infected, also questions were incorporated about the signs and symptoms (based on WUWHS 2008) on which the diagnosis of a chronic wound infection relied on. Additionally, questions were asked about undertaken diagnostic assessments, the type of wound dressings used, and the use of antimicrobials in relation to the existing wound, in the last three months. At patient level, information was collected by the rater pair about demographic characteristics (sex, age, mobility, operation), diseases registered in the medical records, and the degree of care dependency (as measured using the Care Dependency Scale).[14] At ward level, the head of the department filled in an 6-items questionnaire with dichotomous (yes/no) answer categories about specified quality indicators at ward level related to the care of chronic wounds *(Table 3)*. At institutional level, the institutional coordinator filled in an 7-items questionnaire with regard to specified structural quality indicators at institutional level related to the care of chronic wounds. These quality indicators were derived from the original LPZ structural indicators for pressure ulcers and intertrigo.[15]

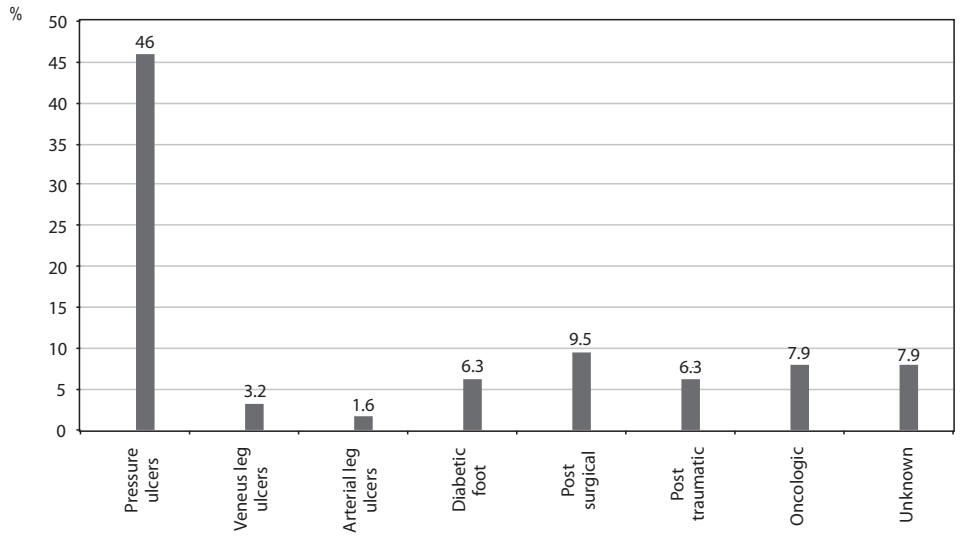
Data analysis
Descriptive analyses were performed with SPSS version 20.0 (SPSS Inc, Chicago, IL, USA).

Results

21 nursing homes with 61 wards agreed to participate in the prevalence measurement of chronic (infected) wounds *(Table 1)*. In total 1514 patients were assessed, which is a response of 96.4% in the participating wards. 67.0% were female and the mean age was 82 years (SD 10.0).

Chronic wounds
63 out of 1514 patients had one or more chronic wounds, which results in a prevalence of 4.2%. These patients had a total of 72 chronic wounds. Almost half (46%) of these wounds were pressure ulcers *(Figure 1)*, followed by post-surgical wounds (9.5%).

Figure 1: Prevalence of the different chronic wounds on the total number of chronic wounds.



The most frequently identified body locations of chronic wounds were the trunk (n=16; 22.2%), hip/thigh (n=11; 15.3%) and the legs of the patients (n=9; 12.5%). Seven (10%) of the chronic wounds were located at the heel or foot. Other locations included 17% of all chronic wounds.

Most chronic wounds existed for a period shorter than 3 months (n=45; 62.5%).

16 out of 72 (22%) of the chronic wounds were considered to be infected. In *Table 1* the different signs and symptoms, used to diagnose these chronic infected wounds, are shown. The wound care nurses or elderly care physicians considered especially an increase of exudate (81.3%; n=13), the existence of erythema (68.8%; n=11), pain (56.3%; n=9) and wound recalcitrance (56.3%; n=9) as relevant clinical signs and symptoms to identify a chronic wound infection *(Table 1)*.

Table 1. Signs and symptoms of infected chronic wounds (n, %) as assessed by the wound care nurses or ECPs.

Signs and symptoms of infected chronic wounds	Infected chronic wounds (n=16)
Pain	9 (56.3 %)
Erythema	11 (68.8 %)
Local warmth	1 (6.3 %)
Swelling	4 (25.0 %)
Induration	0 (0 %)
Smell	0 (0 %)
Increase of (purulent) exudate	13 (81.3 %)
Delayed (or stalled) healing	9 (56.3 %)
Bleeding or friable (easily damaged) granulation tissue	2 (12.5%)

Of all 16 wounds considered to be infected, 5 were managed with an anti-bacterial type of dressing, 4 with some kind of film dressing, 1 with hydrogel, 2 with impregnated fatty gauzes and 3 wounds were covered with 'other' kind of dressings then mentioned specifically *(Table 2)*. The different dressings used for the management of chronic wounds are shown.

Table 2. Dressings used for chronic wound management (n).

Type of dressing	Not infected chronic wounds	Infected chronic wounds
Dry	2	0
Alginate	4	1
Film	0	4
Hydrocolloïd	2	0
Hydrogel	2	1
Foam	6	0
Impregnated fatty gauze	2	2
Negative Pressure Wound Therapy (NPWT)	0	0
Anti-bacterial	1	5
Hydrofiber	6	0
Other	26	3
None	2	0

Quality indicators of chronic wound care

In *table 3 and 4* the results of the structural quality indicators related to chronic wound care at institutional respectively ward level are shown.

Institutional level

Table 3. Quality indicators related to chronic wound care at institutional level (n, %).

Quality indicators	Nursing homes (n=21)
Approved protocol/guideline for prevention and treatment	14 (66)
Patients having a chronic wound for more than 3 weeks are reported to a central contact (e.g. an experienced nurse in wounds or pressure ulcers).	17 (81)
Central registration of the number of patients suffering from chronic wounds.	21 (100)
In the last two years, a training and / or thematic meeting on the prevention and treatment of chronic wounds has been organized.	21 (100)
Information brochure on wounds for patients available.	14 (66)
Standard policy at admission or discharge, with regard to information transfer in the chain care.	20 (95)

In all participating nursing homes, the number of patients with a chronic wound was centrally registered and every two years, a training on prevention and treatment was organised. In 20 nursing homes a standard policy on admission or discharge was available with regard to information transfer to another care provider. However not every nursing home had a protocol/guideline dealing with chronic wounds and/or an information brochure for residents and family on chronic wounds *(Table 3).*

Ward level

In *table 4* the results of the answers with regard to the quality indicators at ward level are shown. Although at institutional level, most structural indicators were fulfilled; at ward level most indicators they were not.

Table 4. Quality indicators related to chronic wound care at ward level in 2012 (n; %).

Quality indicators	Wards (n=61)
Wound care nurse for chronic wounds	7 (11)
Discussion of patients within multidisciplinary meetings	4 (7)
Implementation of a protocol/guideline	8 (13)
Cause of chronic wound is mentioned in the patient record	1 (2)
Preventive measures are mentioned in the patient record	20 (33)
Information brochure on chronic wounds	0
Standard information transfer at discharge	60 (98)

The transfer of wound related information was a normal procedure at discharge of a patient in almost all wards. At 20 wards the preventive measures were mentioned in the patient records, and in only 8 wards a chronic wound protocol was implemented. At 7 wards there was a wound care nurse, specifically taking care for chronic wounds, while discussing patients in a multidisciplinary setting was done in only 4 wards. The aetiology of chronic wounds was listed at one of the 61 wards. Although it has been indicated that institutions had an information brochure on chronic wounds available, it has not been distributed to patients at ward level.

Discussion

To the best of our knowledge, this study measured the prevalence of (infected) chronic wounds in Dutch nursing homes for the first time. The results showed a prevalence of chronic wounds of 4.2% in a Dutch nursing home population of 1514 residents. Nearly 50% of the wounds were located at the trunk or hip/thigh, whereas 46% of all chronic wounds were pressure ulcers. 62.5% of the chronic wounds existed for a period of less than 3 months. Experienced wound nurses and/or ECPs assessed that 22% (n=16) of the 72 chronic wounds were infected. Erythema, exudate, pain and wound recalcitrance were the signs and symptoms they based this diagnosis on. At institutional level all of the measured structural quality indicators scored 66% or more. Except for the chronic wound related information at admission or discharge, all quality indicators scored much lower at ward level. A chronic wound protocol was implemented in only 8 of the participating 61 wards. In 7 of these, a specific wound care nurse took care of chronic wounds, while discussing patients in a multidisciplinary meeting was done in only 4 wards.

Wounds intend to occur more in elderly patients and in those with a poor clinical condition, and are therefore common in nursing homes.[16] Although the impact on the quality of life of patients suffering from a chronic wound has been well documented,[17,18] very little is known of the prevalence of chronic wounds. In an urban population of London (UK), Moffat et al. identified a crude ascertainment of 0,45/1000 population (113/252000) for leg ulceration, with more than 4 weeks duration, with a mean age of 75 (range 31-94 years).[19] Except for the study of Moffat et al. there are no other studies on the prevalence of (infected) chronic wounds.[19] Identification of infection of acute and chronic wounds in daily clinical practice in general is merely based on clinical signs and symptoms.[20] The signs and symptoms of infected chronic wounds are often subtle and a correct diagnosis of infection is difficult to make.[21-26] Using the WUWHS criteria, the experienced wound care nurses and/or ECPs assessed 16 chronic wounds to be infected.[11]

Taken into consideration that the diagnosis of chronic wound infection in itself is difficult [10,11,23,24] and that the nurses and ECPs were not specifically trained, it may be that the number of 16 chronic wounds they assessed to be infected is just an estimation. The consensus document of the World Union of Wound Healing Society shows 'increase of purulent exudate' and 'erythema' as triggers for suspecting a localised infection in an acute wounds.[11] This study showed that the nurses and ECPs still used 'traditional' criteria of wound infection. For Dutch elderly care physicians this was already found in 2009.[10,24]

This study also shows that different dressings were used for the management of (infected) chronic wounds. It is rather striking that in only 30% (5/16) of the wounds, considered to be locally infected, anti-bacterial dressings were used. It is even more striking that in these infected wounds, film dressings, hydrogels and impregnated fatty gauzes were used, not having any antimicrobial capacity at all. Off course, one has to be cautious not to draw any premature conclusions, because of the small numbers involved.

In this study 21 nursing homes and 1514 patients participated. This is a small part of the 345 (in 2003) nursing homes with about 63,000 residents in the Netherlands. The measured prevalence of 2.4% for chronic pressure ulcers in this study was comparable with the prevalence of pressure ulcers existing for more than 2 weeks measured by Halfens et al, for a much larger population of care home residents in The Netherlands.[15] Although the sample of the present study is relatively small and the participating nursing homes were mostly located in two southern provinces of the Netherlands (Brabant and Limburg) the distribution between countryside and cities was even. The resemblance of the chronic pressure ulcer prevalence between the present study and the one of Halfens, leads to the careful impression that the results of this study are representative for all 345 nursing homes in the Netherlands. Indeed, in this study, pressure ulcers were the mostly occurring chronic wounds and because the characteristics (gender, age and BMI) of both Halfens' [15] and our study population are virtually the same, the representativeness of the results of the present study for all nursing homes in the Netherlands is enforced.

The burden of chronic wounds is unknown in most health economics, due to the wide variation in definition and management of chronic wounds.[27] Therefore in 2010 Fletcher argued the necessity of a consistent methodology, and an on-going surveillance system for the UK.[27] In the Netherlands, from 2012, an on-going surveillance is set up by the LPZ, measuring the prevalence of (infected) chronic wounds and related quality indicators, twice a year and always in the same manner. Prevalence data about chronic wounds and the quality of care for patients with chronic wounds, will contribute to the awareness of caregivers, managers, policymakers and politicians. Subsequently, interventions to improve the care for patients with chronic wounds can be initiated. Taken into account the low scores of the structural quality indicators at ward level, development of wound care policy should specifically focus on creating the possibility of conducting a multidisciplinary discussion on (infected) chronic wounds and their registration as part of the patients' treatment plan. For the implementation of adequate measures the appointment of specific ward nurses, and ward physicians with specific knowledge and skills on chronic wounds is warranted.

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Chapter 4

Swab versus biopsy for the diagnosis of chronic infected wounds; a literature review

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ASW.0000428984.58483.aa.Review

Abstract

The goal of this review was to investigate the usefulness of a wound swab (using the Levine or Z-technique) in comparison to a biopsy as a reliable method for the diagnosis of a chronic wound infection.

Method

A literature review using the electronic databases PubMed, CINAHL and Medline were searched by strategy. A total of 6 articles fulfilled the inclusion criteria.

Main results

The Levine technique detects more organisms in acute wounds as well as in chronic wounds, than the Z-technique. Comparing both with the biopsy as criterion standard, the diagnostic accuracy to diagnose a chronic wound infection by the Levine's technique was higher in comparison to the Z-technique. At a threshold of $3.7x10^4$ micro-organisms per swab, the Levine's technique had a sensitivity of 0.90, a specificity of 57%, and a positive predictive value and negative predictive value of 0.77 and 0.91, respectively. Description of the method of swab taking was diverse and not uniform.

Discussion

Only a few studies in the literature compare wound swabs and biopsies for the diagnosis of chronic infected wounds. Until now, the Levine technique has been considered as the most reliable and valid method, but there is an urgent need for a well-designed study with a sufficient number of patients to optimize the diagnostic accuracy of chronic infected wounds.

Conclusion

The best sampling technique for taking a swab has not yet been identified and validated. Until than the authors recommend the Levine technique.

Keywords: chronic wound infection, bacterial quantification, culture technique.

Introduction

In general, a wound can be defined as a break in the continuity of tissue structure. A cutaneous wound can be described in terms of erosion, ulcer, or fissure.[1] When wounds proceed through the healing process in an orderly and timely manner and achieve anatomic and functional integrity, they are considered to be acute wounds. If wounds do not achieve this healing process, they are considered to be chronic.[2]

Chronic wounds are often painful and debilitating and thereby result in extreme loss of quality of life. Direct costs of chronic wounds to the United Kingdom's National Health Service are estimated £2 billion to £3 billion per year.[3] In the United States, chronic wounds annually affect 6.5 million patients, which are estimated to cost in excess of US $25 billion.[4]

Knowledge of both intrinsic and extrinsic factors that may contribute to wound recalcitrance is essential to perform successful wound care. Only when the correct causative factor(s) has/have been established can an effective treatment plan be set up.[5,6] Wound recalcitrance is mostly due to secondary factors, such as vascular insufficiency and infection.[7] Wound infection implies multiplication of micro-organisms within the wound resulting in a prolonged (and excessive) inflammatory response, a delay in collagen synthesis, retarded epithelialization, and finally in tissue damage.[8-11]

A controversy exists regarding the role of micro-organisms in the pathogenesis of chronic wound infection.[12] The absolute number of micro-organisms may be less important than the collaboration of micro-organisms in a biofilm, creating the potential of quorum sensing to increase their individual virulence and persistence.[10]

Accurate identification of infections of acute and chronic wounds is challenging and usually based on clinical signs and symptoms. In contrast to the overt signs and symptoms of acute wounds, the signs and symptoms of a chronic wound infection are often more subtle, and therefore, the diagnosis is difficult to make.[12-17]

To date, bacterial quantification has been proposed as a potential technique to diagnose wound infections.[18] Microbial growth greater than 10^5 colony-forming units (CFUs)/g tissue or mL wound fluid has been suggested as indicative for wound infection.[18-22] Methods to determine the bacterial burden are quantitative culturing of wound swab, tissue biopsy, wound fluid obtained after curettage, or fine-needle aspiration.[23,24] Time requirements, expert technician processing, and the introduction of a trauma have made tissue biopsy not popular for both the patient and the professional.[25,26] Yet, quantitative culturing of tissue biopsy is considered as the criterion standard.[26-29] Another method involves taking wound swabs and is less time consuming and cost-effective and moreover, it is non-invasive.[27,30-33] The most common swab techniques are the Levine and the Z-technique. The Levine technique involves rotating the wound swab over a 1-cm^2 area of the wound for five seconds, with sufficient pressure to extract fluid from the inner part of the wound; the Z-technique involves rotating the swab in a zigzag fashion covering the entire injured area across the wound, without touching the wound edges.[32,34-36]

Nevertheless, conflicting information continues concerning 'the best practice in taking a wound swab'.[35] Consensus regarding the methodology for taking a swab has not been defined to date yet.[37-41] This review strives to answer the question of whether a wound swab using the Z- or the Levine technique in comparison to a biopsy is a valid and reliable method for the diagnosis of a chronic wound infection.

Methods

Between the dates of January 1, 2005 and August 15, 2011, Electronic databases PubMed, CINAHL, and Medline were searched for human studies using the following search strategy: smear OR smear microscopy OR microbiological techniques OR bacteriological techniques OR clinical laboratory techniques OR biopsy OR culture media OR culture techniques OR wound biopsy OR wound swab OR wound OR wounds and injuries OR wound infection AND wound OR wounds and injuries AND wound infection was used. It was not within the scope of this review to include animal studies. The search in PubMed and CINAHL yielded one overlapping article. The selection of 2332 articles was screened by title. Inclusion followed when a swab or biopsy was mentioned in the title and compared with a reference standard. When the title indicated procedure aspects for swab taking, they were also included. Using the same selection criteria, the series of references of the selected articles were searched for relevant titles. Finally, 49 articles were selected *(Figure 1).*

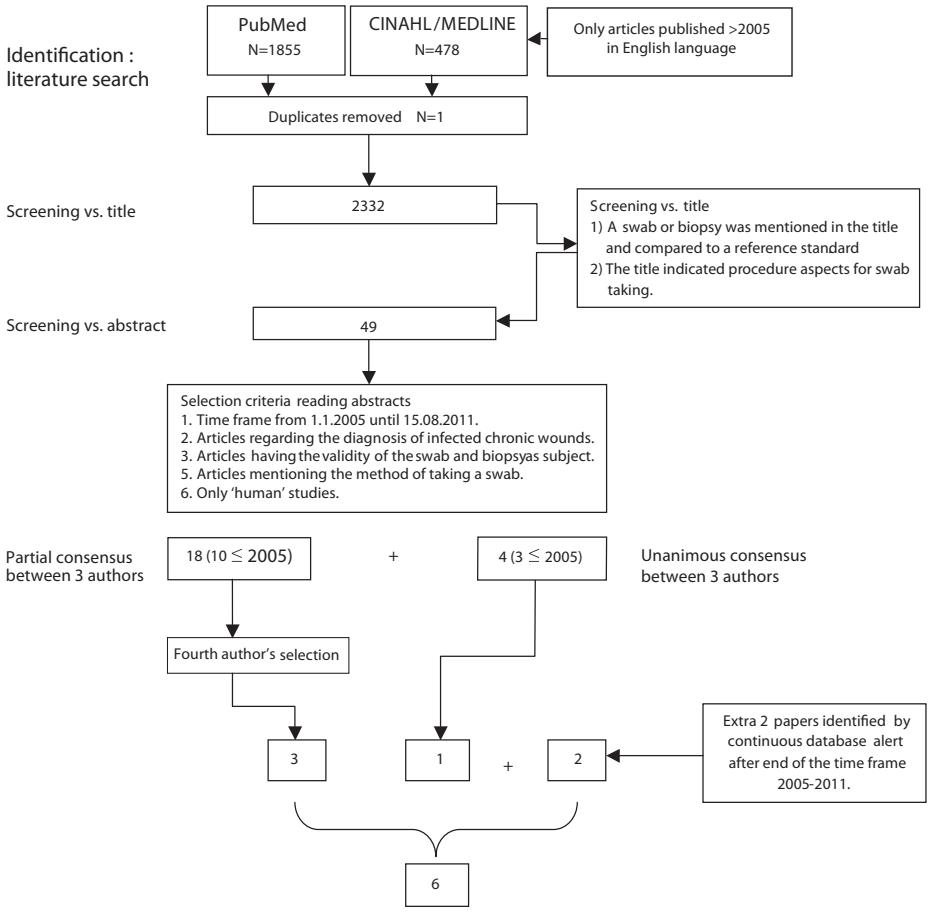
From those articles A.R., E.S. and J.S. selected independently those articles articles deemed relevant by reading their abstracts and taking into account the following specific inclusion criteria: articles should concern the diagnosis of infected chronic wounds or have the validity of the swab or biopsy as the subject. In addition, articles that mentioned a method of swab taking were also included *(Figure 1).*

The authors maintained a unanimous consensus on the inclusion of 4 articles. Unfortunately, 3 of the articles were published before 2005. Finally, 4 articles were chosen for inclusion in this review. Subsequently, a continuous monthly database alert was set up, using the same search strategy and inclusion criteria, leading to 2 more published articles beyond the date of the original time frame and bringing the final selection to 6 articles.[42,43]

Results

Clear diversity in the type of the 6 selected articles was found. The selection consisted of 3 reviews, 1 randomized controlled trial (RCT) and 2 cross-sectional studies. Successively, the following issues will be described in this Results section: diversity of the samples, the different types of included wounds, and the way in which wound infection was assessed. In addition, swab taking will be compared to the biopsy as criterion standard, and finally, the method of the swab taking will be explored. A summary of relevant findings of the selected articles is presented in the *Table 1* page 53.

Figure 1



Sample and setting

Patients in the RCT and the 2 cross sectional studies were recruited within different settings , for example, a university teaching hospital, a department of a Veteran's Affairs Medical Center, and a university based multidisciplinary chronic wound center.[35,43,44]

Type of wounds

Recruited patients of the included studies had a variety of chronic wounds *(Table 1)*. Only 1 author mentioned specifically the duration of the wounds of the patients included.[45] The other authors did not disclose the exact duration of the chronic wounds that were included.[35,43]

Criteria of wound infection

The presence of infection was assessed by different methods in the studies, either by white blood cell counts >1,500 cells/mm^3 (n=1), the outcome of quantitative analysis, and presence of bacteria greater than10^5 CFU/g tissue (biopsy) or greater than 10^5 CFU/cm^2 (swab) (n=1) or by assessing the presence of clinical signs and symptoms (n=3).[35,42,43,45] Two of the 6 authors specifically indicated the different clinical signs and symptoms on which their diagnosis of wound infection was based. [42,43] Angel et al.[43] made use of the criteria mentioned in the international guidelines of the European Wound Management Association and the World Union of Wound Healing Societies to diagnose wound infection in the patients included in their study.[14,15,46]

Swab technique used

The 2 cross-sectional studies and the RCT used the Levine technique, or a combination of both techniques, to compare with a biopsy. The Levine technique is the preferable method to take a swab, as is indicated by the 3 included review articles.[25,42,45]

Swab versus biopsy for infected chronic wounds

Bonham[33] concluded a maximal concordance of 62-72% in results between swab and biopsy.[33,47,49] Drinka et al.[42] referred to Pellizzer, who compared swab specimens to biopsies and found 2.34 isolates per patient using a swab and 2.07 with a biopsy in 29 severe diabetic foot ulcers and argued that taking a swab or biopsy may be equally reliable.[50] Referring to the comparison of the Levine technique and Z-technique, the study of Angel et al.[43] showed that the Levine technique was able to detect more organisms in acute as well as in chronic wounds. In contrast, by referring to the study of Bill et al.[27], O'Meara et al.[45] suggested that wound swabbing is not a useful test. Bill et al.[27] compared 38 patients' quantitative swabs taken by the Levine technique with a quantitative biopsy as criterion standard and concluded that the Levine technique had a sensitivity of 79% and a specificity of 60%. Comparing the different swab techniques with the biopsy as criterion standard, Gardner et al.[35] concluded that the diagnostic accuracy to diagnose a chronic wound infection by the Levine technique was higher in comparison to the Z-technique. At a threshold of $3.7x10^4$ micro-organisms per swab, the Levine's technique had a sensitivity of 0.90 and a specificity of 57%, and the positive predictive value and negative predictive value were 0.77 and 0.91, respectively.[35]

Method of swab taking

In 3 of the 6 studies the type of swabs used was mentioned, a Culturette swab (Becton Dickenson, Cockseyville, Maryland), a Dryswab (Medical Wire and Equipment Co. Ltd, Corham, United Kingdom) and a cotton tipped swab.[35,43,44] The discipline of the professional(s) responsible for collecting the swabs was mentioned in the study of Angel et al.,[43] who indicated that the swabs were collected by 2 specially trained and qualified nurses. Four authors suggested to first cleanse the wound bed with sterile 0.9% saline before taking the swab, whereas Davies et al.[44] irrigated the wound bed with sterile saline before culturing the swab.[27,35,42,43] Drinka et al.[42] mentioned that the wound should be free of necrotic material, eschar, purulence, or drainage before taking a swab. Several authors first took a swab from the wound and successively cleansed the wound again to take a biopsy.[35,44,45] Angel et al.[43] stated an exact time frame of 5 minutes between taking the Levine and Z-technique swabs. The order of swab taking by Angel et al.[43] was randomized by the flip of a coin. The collected swabs were usually transferred to the laboratory within 2 hours after collection for processing. Some did not mention the time frame between collecting and analyzing the sample.[42,43]

Table 1. A summary of relevant findings of all selected articles

Citation	Bonham[33] (2009)	Davies et al[44] (2007)	Gardner et al[35] (2006)	O'Meara et al[45] (2006)	Angel et al[43] (2011)	Drinka et al[42] (2012)
Aim of the Study	To examine research and published expert opinion about swab cultures for the diagnosis of wound infection	To determine prospectively whether a relationship exists between the composition of the wound microflora and healing. Second, to assess the clinical usefulness of tissue biopsies in comparison with swabbing of the wound surface, in both characterization of the microflora and subsequent management of these patients	To address the limitations of previous studies by delineating and fully describing the swab techniques that were studied and compared, comparing the swab technique against the reference standard method of specimen collection (i.e., biopsy of "viable" wound tissue)	To use systematic review methods to summarize the evidence on the diagnostic performance of (1) clinical examination, (2) microbiological sampling techniques, and (3) methods for microbiological analysis of the wound sample in diabetic patients with foot ulcerations	To compare 2 wound swabbing techniques (Levine vs. Z- technique) to establish which method is more effective in determining the causative organism(s) in infected cutaneous wounds	The study is focused on swab culture obtained by the Levine technique, after debridement or cleaning down to viable tissue when an acute purulent skin infection has been diagnosed based on clinical criteria
Design, Sample, Mean Age, Setting, and Type of Wounds	**Design:** Review	**Design:** Observational study with cross-sectional design	**Design:** Observational study with cross-sectional design	**Design:** Review	**Design:** RCT	**Design:** Review
	Sample, mean age, setting, and type of wounds: None	**Sample:** 70 patients were selected on clinically noninfected venous leg ulcers, with a mean duration 40 mo (range, 1-204 mo), and mean surface of the wound of 1996 mm^2	**Sample:** 83 patients, with a white blood cell (WBC) count >1500 cells/μL or total lymphocyte count >800 cells/μL, platelet count >125,000/mm, no coagulopathies, and not receiving anticoagulation therapy	**Sample:** 38 patients with a cutaneous wound at any body site, present for at least 6 mo (Bill et al.,[27] 2001)	**Sample:** 50 patients were recruited from both an inpatient and outpatient setting of an 855-bed university teaching hospital in Perth.;28 males and 22 females, with a mean age of 62.46y. Acute wounds accounted for 42%, chronic wounds for 58%.Order of swab collection was randomized by the flip of a coin	**Sample, mean age, and setting:** None
		Mean age: Mean age of 72 y, with a range from 20-90 y of age	**Mean age:** Mean age of 57 (SD, 11.6)	**Mean age:** Mean age of 59 y	**Mean age:** 62.46 y	
		Setting: Wound Healing Research Unit, University Hospital of Wales, Cardiff	**Setting:** A Department of Veteran's Affairs Medical Center and a university-associated tertiary hospital	**Setting:** University based, multidisciplinary chronic wound center	**Setting:** University teaching hospital in Perth, Western Australia	
		Type of wounds: Noninfected chronic venous leg ulcers	**Type of wounds:** Nonarterial chronic wounds	**Type of wounds:** Chronic cutaneous wounds lasting for at least 6 monds	**Type of wounds:** Acute wounds accounted for 42% and chronic wounds for 58%, with a different etiology, ie, leg ulcers, venous, arterial, and mixed as well as diabetic and pressure ulcer	**Type of wounds:** Skin and soft-tissue infections in nursing homes that develop within a chronic wound

Main Results	Although swab cultures are commonly performed, standardized procedures are lacking. For the swab culture to be accurate, attention to the technique is critical. Essential elements: swab viable and not necrotic tissue eschar or pus, debride necrosis as indicated to access viable tissue, cleanse the wound prior to swabbing, apply sufficient pressure on the swab to express fluid from the wound tissue, use sterile techniques, obtain appropriate supplies and culture media, ensure prompt transportation of the culture to the laboratory, provide complete labeling and precise description of the specimens and forward to a laboratory capable of quantitative processing of the sample	The deep tissues of all noninfected wounds contained bacteria (mean isolates per wound 2.80; range, 1-6), and the swab specimen yielded a mean of 2.74 isolates per wound (range, 1-6). Its presence on the surface was substantially associated with the presence in the deep-tissue biopsy for aerobes, but not for anaerobes The presence of ≥4 bacterial genera on the surface of the wound or in the tissue, showed an important inverse relation to healing	Treatment with systemic antibiotic treatment was associated with having a noninfected wound (p= 0.011). There was a significant difference in wound size between the infected and noninfected groups (P = .009).The concordance between Levine technique and tissue specimens was 78%. A sensitivity value of 90% and a specificity of 57% for the Levine technique at the threshold of 3.7 x 10^4 organisms per swab. With a positive predictive value of 0.77 and a negative predictive value of 0.91	The estimated sensitivity for wound swab was 79%, and specificity was 60%, suggesting that wound swabbing is not a useful test	Different species of organisms were detected in both acute and chronic wounds with both the Levine and the Z- technique. Anaerobic organisms were detected only in chronic wounds (VLU), by both methods of specimen collection. Majority of chronic wounds were polymicrobial. The Levine technique detected more organisms in chronic wounds (t = 12.04, P < .001). When the acute and chronic group of wounds were combined, the Levine technique detected more organisms (t = 15.46, p ≤ .001)	Swab culture should not be used to determine if the wound is acutely infected but rather the role is to identify potential pathogens in a wound that is acutely infected based on clinical assessment when deep tissue biopsy is not elected
Citation	**Bonham[33] (2009)**	**Davies et al[44] (2007)**	**Gardner et al[35] (2006)**	**O'Meara et al[45] (2006)**	**Angel et al[43] (2011)**	**Drinka et al[42] (2012)**
Used Criteria of Wound Infection			Selection of patients who had a WBC count >1,500 cells/μL or total lymphocyte count >800 cells/μL	Soft tissue infection was defined as the presence of $>10^5$ CFUs/g tissue or 10^5 CFU/cm^2 for swab cultures	Acute wound infection was defined as inflammation present for >5 d, purulent discharge, elevated temperature >38°C, spontaneous dehiscence or presence of an abscess. Criteria of chronic wound infection were increased exudate, presence of odor, erythema >1-2 cm, warmth around the wound, poor quality granulation tissue, pain or tenderness of the wound site, or no improvement in the preceding 2 wk in a clean wound	Diagnosis of infection was based on clinical criteria

Swab Technique	**Levine:** A guideline to perform wound cultures using the Levine 1-cm[26] swab method is proposed	**Levine:** Wounds were irrigated with sterile saline and the wound bed was sampled via a surface swab of a 1-cm^2 area from the center of the wound	**Levine and Z-technique:** Concurrent swab specimens were obtained using wound exudates, Z-technique and Levine technique. Samples were gathered, after gently cleansing with a nonbacteriostatic saline, with a Culturette swab	**Levine:** A sterile 4x4-cm gauze was moistened with sterile saline, and the wound service was wiped vigorously to remove surface contamination. Using sterile technique, an alginate tipped applicator was rotated over a 1x1 cm for 5 s with sufficient pressure to cause tissue fluid to be expressed. The sample was obtained from the center of the wound. The tip of the swab was then broken off into a sterile transport tube containing 5 mL of saline. Subsequently, a tissue biopsy was taken from the center of the wound	**Levine and Z-technique:** Swabs were collected by the Z-technique and Levine technique, from the same wound, no more than 5 min apart. Prior to collection the wound was cleansed once with sterile 0.9% normal saline. Sterile, premoistened cotton-tipped swabs, with sterile 0.9% normal saline, were used. All swabs were collected by 2 trained and certified nurses	**Levine technique:** Proper technique to obtain a swab is important. Poor technique is often used
Remarks			Patients suffered full-thickness, nonarterial chronic wounds Patients with low white blood counts were excluded to reduce the risk of wound infection related to tissue biopsies	With regard to the sensitivity and specificity of a wound swab, this systematic review referred to the article of Bill et al.[27] (only)		The relative value of Levine swab culture vs empiric systemic antibiotic use on the outcome of mild acute wound infection in the nursing home, is said to be unknown, since neither approach has been tested. Clinical criteria of infection are not mentioned

Discussion

In the authors' quest to determine whether a wound swab using the Z- or the Levine technique in comparison with a biopsy is a valid and reliable method for the diagnosis of a chronic wound infection, the specific research question and the time period in which the search was made differed from earlier reviews.[33,42,45] Although the primary objective of the study was to focus on chronic wounds, it was clear in advance that a systematic search would not elicit many hits. The use of inconsistent wound infection criteria made it even more difficult to draw a conclusion. Based on the analysis of 6 out of the 2333 articles, the authors found that the Levine's technique is, to date, the most valid diagnostic method to demonstrate infection of a chronic wound.

The concordance reported by Bonham of 62 to72% between swab and biopsy depends on some references that did not describe the sampling technique used.[33,47-49] Davies et al.[44] selected patients with clinically non-infected venous leg ulcers for their study. It is therefore not possible to draw a conclusion about the validity of the swab for assessing chronic wound infection. Gardner et al.[35] concluded that the diagnostic validity of the Levine's technique was higher than that of the Z-technique, when compared with the quantitative results (>1x10^6 CFUs/g of tissue) of a biopsy. But the sample was limited to 30 chronic wounds, whereas their 'true' infection status was based solely on the quantitative culture finding from tissue specimens.[35] Angel et al.[43] compared the Levine technique and Z-technique by recruiting 29 patients with various types of clinically infected chronic wounds, -leg ulcers, including venous, arterial, mixed, diabetic, and pressure ulcers. They used the existing international guidelines to determine wound infection when recruiting patients and did not use the biopsy as criterion standard.[14,15,43] Angel et al.[43] are among the first authors to extensively describe the procedure of swab taking. Regarding the strategy oftaking a swab, some authors suggest to cleanse the wound bed before swab taking.[41,51] Others advise the specific use of sterile 0.9% saline for cleansing.[6,52]

Moreover, the use of antiseptic solutions for cleansing has been discouraged.[53,54] However, it is not clear whether surface contamination, topical therapies such as creams or residual iodine, loose tissue detritus, and gross exudate should be removed prior to sampling. Because the taking of a swab or biopsy concerns the wound itself, it would appear cogent to remove any surface contamination before swab taking, as far as practically possible, without unduly disturbing the wound surface.[36,40] Although premoistening of a swab can improve yields when sampling a dry wound surface, the swab taking of a desiccated wound is seldom indicated.[41] Uppal et al.[55] preferred to moisten a dry swab, but exclusively included (acute) burns. In the past, some swabs were serum-coated to help the survival of organisms during transport, but because the great majority of wounds tend to produce at least some exudate, it has been argued that this coating is not necessary.[40] In addition, because fatty acids contained in cotton swabs can inhibit bacterial growth for some fastidious organisms, some authors prefer to use an alginate or rayon-tipped swab instead of cotton-tipped swabs, obviating the need for extraction if quantitative bacteriology is contemplated.[27,40,41,45] The discussion about swab taking is further complicated by the fact that more than 50% of all chronic wounds have biofilm.[56,57] The practical inability to exert pressure on the wound bed with the Z-technique in comparison with the Levine technique is responsible for the detection of less planktonic bacteria with the Z-technique.[43]

This is in contrast to the latest recommendation to execute downward pressure with the Z-technique as well, causing the release of fluid from the wound surface.[36]

Earlier, Robson et al.[20] concluded that for efficient wound healing of acute postsurgical wounds, any bacterial count must be less than 10^6 CFUs/mL. In contrast, the '10^5 guideline' as an indicator for chronic wound infection has been disputed, and the swab taking may solely reflect bacterial colonization or even intact skin.[12,22,27,32,41,58] For chronic wound infection, Bowler[22] stressed the necessity of microorganisms to adapt and to overcome the host immune response. Therefore, the absolute number of micro-organisms may be less important than the potential of quorum sensing to increase their virulence and persistence.[10] A specific target number of bacteria for chronic wounds, demanding anti-bacterial treatment, is therefore debatable. Thus, although they are sometimes subtle and difficult to interpret, signs and symptoms currently are more useful to diagnose a chronic wound infection.

There are only a few studies comparing wound swabs with biopsies for the diagnosis of chronic infected wounds. To date, the Levine technique has been considered the most reliable and valid method of swabbing. Nonetheless, an urgent need exists for a well-designed study with a sufficient number of patients to optimize the diagnostic accuracy of chronic infected wounds. Although some recommendations can be made, the best sampling technique for taking a swab has not yet been identified and validated.

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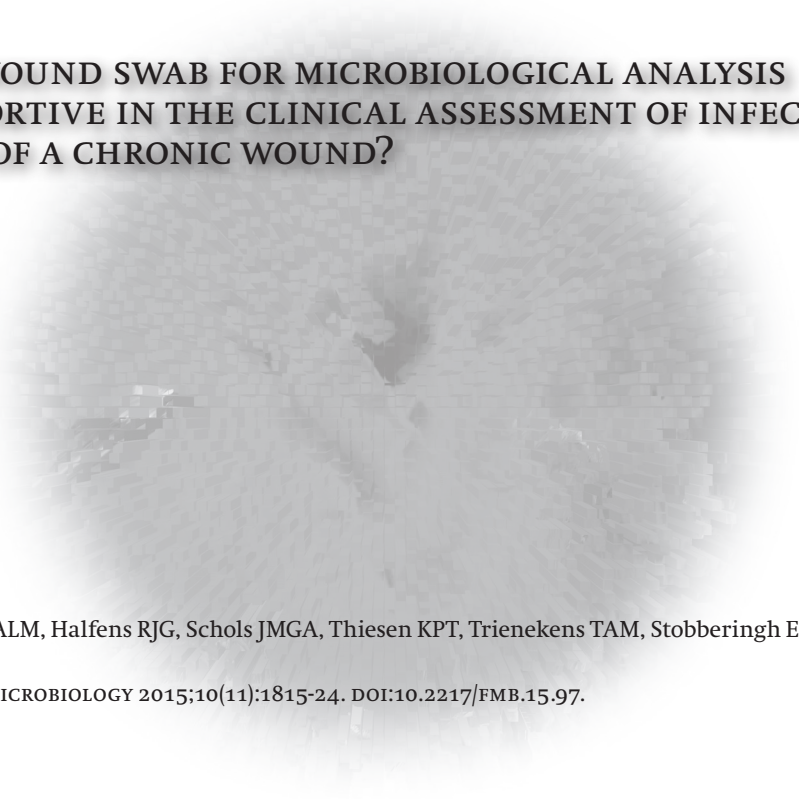
Chapter 5

Is a wound swab for microbiological analysis supportive in the clinical assessment of infection of a chronic wound?



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Introduction

The outcome of the interaction between the human host and the bio burden of the wound is not readily predictable. When the host's immunological competence is compromised and/or microbes manifest stronger virulent factors, overt wound infection may occur. The microbial invasion into the host's tissues leads to cellular damage, immunological responses and the development of clinical signs and symptoms.[1,2] Wounds are considered chronic if they do not reach complete epithelialisation and functional integrity within three weeks.[3,4] Chronic wounds are often painful and debilitating and can lead to a reduction in quality of life.[5-8] In contrast to the overt signs and symptoms of infection in acute wounds (pain, erythema, edema, heat and purulence), the signs and symptoms of infection in chronic wound are more subtle, making the diagnosis of infection more challenging.[9-11]

Because microorganisms are present in all wounds healing by secondary intention,[12] it has been argued that the distinction between colonisation and infection has to be considered both clinically and microbiologically. However, studies addressing the distinction between colonisation and infection in chronic wounds are limited. Only one study has compared microbiological findings between infected and non-infected ulcers to assess which microbes are associated with infection. Though the authors reported that ulcers that were clinically assessed as infected had significantly more positive swab cultures than non-infected ulcers, they failed to define a positive swab culture and did not mention the microorganisms that were cultured.[13] Although evidence-based consensus is lacking, the Levine technique is currently the most preferable way for taking swabs of chronic wounds.[14-15] In 2008, the World Union of Wound Healing Societies (WUWHS) published an international consensus document to provide an overview of the current clinical practice in relation to wound infection. Different diagnostic signs and symptoms of infection were proposed for acute and chronic wounds.[16]

Consensus on the presence of reliable and relevant indicators to differentiate between an infected and a non-infected chronic wound is essential for careful antimicrobial treatment and efficient management of these wounds, as well as for reducing negative economic, health and care consequences.[17] That is why this study examines whether a microbiological assessment done through swab taking supports the clinical assessment, which is based on the signs and symptoms proposed by the WUWHS.[16]

The clinical assessment of the chronic wounds of patients suffering from diabetes or peripheral arterial disease (PAD) is given special attention, for it is assumed that diabetic foot infections will continue to occur more frequently because of the increasing rate of diabetes, which is expected to rise to 522 million (9.9%) by 2035.[18] In addition, the wounds of patients suffering from diabetes or PAD are more difficult to assess clinically for infection because advanced patient age, poor tissue perfusion and oxygenation, and elevated blood sugars, reduce the host's inflammatory response to a microbiological invasion.[19]

The aims of this study are:

- To compare the clinical assessments of infected chronic wounds with the microbiological results of cultures taken by a swab.
- To specifically compare the clinical assessments and swab results for chronic wounds of patients suffering from diabetes mellitus or peripheral arterial disease (PAD).

Keywords: Wounds, chronic wounds, wound infection, infection, clinical diagnosis, swab, wound assessment.

Methods

Design

The study was carried out between January and August 2013 as an open, non-randomised study, in an outpatient wound clinic in Venray, the Netherlands. Patients suffering from chronic wounds were assessed for the 13 signs and symptoms of chronic wound infection as mentioned in the international consensus document on wound infection of the WUWHS.[16] Using the Levine technique, a standardised wound swab was taken from each chronic wound at the clinic by two of the authors (AR and ES), who are experienced healthcare professionals, and was given for microbiological analysis.[20]

Patient population and sample

- Inclusion criteria:
  Patients eligible for inclusion were those who had a wound for more than three weeks and who were 18 years or older. After giving their oral informed consent, patients were included.

- Exclusion criteria:
  Patients were excluded when they were terminally ill or suffered from a systemic infection and needed acute hospitalisation.

- Multiple wounds:
  When patients had multiple wounds, each wound was included separately.

- Sample size calculation:
  This study was populated to determine the sensitivity of the symptoms with the 99% confidence level, not extending the anticipated symptom sensitivity of 60% by more than 1%. We used an alpha of .01 to account for the type I error due to multiple symptoms and a beta of 80%. It was calculated that 70 chronic wounds clinically assessed as infected would be needed.[21]

Study variables

For each included patient, age (yrs), sex (m/f), the presence of diabetes mellitus and peripheral vascular disease (PVD) (Y/N), and the location of the wound(s) were registered. Chronic wounds were classified and registered as post-traumatic, leg ulcer, diabetic ulcer, pressure ulcer, oncologic ulcer or burns. Leg ulcers were additionally examined by determining the patient's Ankle Brachial Pressure Index (ABPI).[22-25] The ABPI confirmed the clinical assessment of whether a leg ulcer was venous (ABPI >0.8), mixed (ABPI 0.6-0.8) or arterial (ABPI <0.6) of origin *(Table 1)*.

Furthermore, the following signs and symptoms of a localised and/or spreading chronic wound infection according the WUWHS (2008) were registered (Y/N): 'delayed healing', 'new, increased or altered pain', 'redness', 'heat', 'edema', 'induration', 'odour', 'wound exudate', 'bleeding granulation tissue', 'discolouration of granulation tissue', 'pocketing of the wound base', 'bridging', 'crepitation' and 'lymphangitis' *(Table 2)*. The nurses at the wound clinic were specially educated and provided with example photographs for a better recognition of these signs and symptoms of infection. For practical benefits, the symptom 'new, increased or altered pain' was divided into two different symptoms: 'pain/more pain' and 'new pain' *(Table 2)*.[16] According to the criteria of the WUWHS, chronic wounds have to show one of the highly indicative symptoms or at least two of the other signs and symptoms to be assessed as infected *(Table 2)*.[16] Local use of antiseptics and systemic use of antibiotics up to two weeks before the clinical assessment of the chronic wound was noted (Y/N).

Swabs

Together with the clinical assessment of the chronic wound, the swabs for microbiological analysis were taken (one per wound) during patients' first visit to the clinic between January and August 2013. The swabs were taken after sharp debridement and cleansing of the wound with tap water.[15,26,27]

Table 1: Patient and chronic wound characteristics.

Patients	**n (%)**
Number of patients	192
Age (mean, SD)	74,2 (14,2)
Sex, female (%)	48
Diabetes	56 (29)
Peripheral arterial disease	42 (22)
Wounds (n=211)	**%**
Diabetic foot	8
Pressure ulcers	23
Post-traumatic	20
Post-surgical	14
Leg ulcers	34
Oncologic ulcers	1
Burns	0

A standardised protocol based on the Levine method for swab taking was used to ensure the swabs were taken in a consistent manner and to minimise variation among healthcare professionals.[28] After sampling, each swab was put in Amies gel transport medium (109C USE, single wooden swab, Copan) kept at 4°C and sent to the microbiological laboratory where it was processed within 24 hours for semi-quantitative analysis according to established microbiological protocols.[26,28,29] For the semi-quantitative analysis, the results were assessed as negative, scant (+/-), low (+), moderate (++), and heavy (+++). For the qualitative analysis, the microbiological result was considered negative when no micro-organisms were isolated, and positive when classified as scant (+/-) or more. Then, further identification and assessment of the amount (+,++,+++) of the isolated micro-organisms took place (= quantitative analysis).

Statistical analyses

All data analyses were performed using SPSS (IBM SPSS Statistics 20). The analyses were done on the wound level, first for all wounds, and thereafter specifically for wounds of patients with a known diagnosis of diabetes mellitus or PAD. The chi-square (χ^2) test was used to assess the association between the clinical assessment and the qualitative and quantitative microbiological results. A p-value of <0.05 was defined as statistically significant.

Ethical consideration

The study protocol (METC 12-3-120.4) was approved by the Medical Review Ethics Committee (MEC) (Medisch Ethische Toetsings Commissie – METC) of the Maastricht University Medical Centre (MUMC).

Results

Characteristics

I Patients

Of the patients in the wound clinic, 192 were included in this study. All consecutive patients visiting the clinic fulfilled the inclusion criteria and were willing to participate; therefore no patients had to be excluded. The male to female ratio was 52:48. The mean age of the patients was 74.2 years (SD 14.2). Of the 192 patients, 56 (29%) were diabetic and 42 (22%) were diagnosed with PAD *(Table 1)*.

Table 2: Signs and symptoms of chronic wound infection according to the consensus document of the WUWHS.

Chronic wounds: signs & symptoms of localised and spreading infection
Delayed healing*
Pain/more pain*
New pain*
Redness
Heat
Edema
Induration
Odour
Wound exudate
Discolouration of granulation tissue
Pocketing of the wound base
Bridging
Crepitation
Lymphangitis

* highly indicative symptoms

II Wounds

The 192 patients had a total of 211 chronic wounds (with a mean of: 1.1 wounds per patient) that were included in the study. More than 78% of the wounds were located on the lower leg, feet and toes. The most frequent types of wounds were leg ulcers (30%), pressure ulcers (26%) and post-traumatic ulcers (23%) *(Table 1)*.

III Bacteria

Independent of the type of chronic wound, *Staphylococcus aureus* (44%), *Streptococcus haemolyticus (12%)*, *Pseudomonas aeruginosa (6%)* and *Escherichia coli (5%)* were the most frequently isolated microorganisms. Anaerobes (gram-negative rods and gram-positive cocci together) were isolated in 2% of wounds. Other bacteria species were isolated in less than 1% of wounds.

Statistical analyses

A. All wounds

Of the 211 chronic wounds, 90 (51%) were clinically assessed as infected, while 175 (83%) wounds had a positive swab result. No significant relationship was found between the clinical assessments and the results of the swabs (all Chi square p-values >0.05; *(Table 3)*.

Table 3: Clinical assessment vs. microbiological assessment.

Swabs taken (n=211) of 192 patients 1	**Positive clinical symptoms n (%)**	**Negative clinical symptoms n (%)**	**Total n (%)**
Swab result pos.	73 (81,1)	102 (84,3)	175 (82.9)
Swab result neg.	17 (18,9)	19 15,7)	36 (17.1)
Total	90 (42,7)	121 (57,3)	211
Swabs taken (n=69) of 56 diabetic patients 2	**Positive clinical symptoms n (%)**	**Negative clinical symptoms n (%)**	**Total n (%)**
Swab result pos.	21 (84,0)	38 (86,4)	59 (85.5)
Swab result neg.	4 (16,0)	6 (13,6)	10 (14.5)
Total	25 (36,2)	44 (63,8)	69
Swabs taken (n=57)of 42 PAD patients 2	**Positive clinical symptoms n (%)**	**Negative clinical symptoms n (%)**	**Total n (%)**
Swab result pos.	17 (77,3)	28 (80,0)	35 (61.4)
Swab result neg.	5 (22,7)	7 (20,0)	22 (38.6)
Total	22 (38,6)	35 (61,4)	57
Swabs taken, no antimicrobials (n=68) 3	**Positive clinical symptoms n (%)**	**Negative clinical symptoms n (%)**	**Total n (%)**
Swab result pos.	28 (82.4)	30 (88.2)	58 (85.3)
Swab result neg.	6 (17.6)	4 (11.8)	10 (14.7)
Total	34 (50.0)	34 (50.0)	68

Quantitative analysis showed the same bacterial species, regardless of whether the wounds were clinically assessed as infected or not. Independent of the type of wound, *Staphylococcus aureus* was isolated most frequently. 'Pain/more pain no' and 'new pain no' were significantly (p-value<0.05) correlated with the quantitative swab results for both species *Pseudomonas aeruginosa* and *Enterococcus faecalis* (Chi square, *=p-values <0.05, *Table 4*). No other significant correlations between the clinical assessments and the quantitative swab results were found (Chi square p-values >0.05, *(Table 4)*.

Table 4: Quantitative analysis of swabs taken. Type and frequency of bacteria related to the clinical assessment of chronic wound infection, for all patients and for patients suffering from diabetes or PAD. *Chi-square p-value<0.05.

Bacteria species Total (n=211) Diabetics (n=69) PAD (n=57)	positive symptoms yes n (%)	positive symptoms no n (%)	delayed (or stalled) healing yes n (%)	delayed (or stalled) healing no n (%)	pain/ more pain yes n (%)	pain/ more pain no n (%)	new pain yes n (%)	new pain no n (%)
Staphylococcus aureus +								
all wounds	46 (51.1)	72 (59.5)	36 (50.7)	82 (58.6)	11 (50.0)	107 (56.6)	1 (50.0)	117 (56.0)
diabetics	16 (64.0)	31 (70.5)	12 (57.1)	72,9 (35.0)	2 (50.0)	45 (69.2)	0	0
PAD	11 (50.0)	23 (65.7)	9 (52.9)	25 (62.5)	1 (14.3)	33 (66.0)	0	34 (59.6)
Streptococcus haemolyticus B +								
all wounds	11 (12.2)	15 (12.4)	9 (12.7)	18 (12.1)	1 (4.5)	25 (13.2)	0	26 (12.4)
diabetics	6 (24.0)	9 (20.5)	4 (19.0)	11 (22.9)	1 (25.0)	14 (21.5)	0	15 (21.7)
PAD	0	6 (17.1)	0	6 (15)	0	6 (12.0)	0	6 (10.5)
Pseudomonas aeruginosa +								
all wounds	8 (8.9)	5 (4.1)	3 (4.2)	10 (7.1)	2 (9.1)	11 (5.8)	1 (50.0)	12 (5.7)*
diabetics	3 (12.0)	4 (9.1)	1 (4.8)	6 (12.5)	0	7 (10.8)	0	7 (10.1)
PAD	2 (9.1)	1 (2.9)	1 (5.9)	2 (5.0)	1 (14.3)	2 (4.0)	0	3 (5.3)
Escherichia coli +								
all wounds	7 (7.8)	4 (3.3)	6 (8.5)	5 (3.6)	2 (9.1)	9 (4.8)	0 (0)	11 (5.3)
diabetics	1 (4.0)	1 (2.3)	1 (4.8)	1 (2.1)	0	2 (3.1)	0	2 (2.9)
PAD	2 (9.1)	0	2 (11.8)*	0	0	2 (4.0)	0	2 (3.5)
Proteus mirabilis +								
all wounds	7 (7.8)	13 (10.7)	5 (7.0)	15 (10.7)	3 (13.6)	17 (9.0)	0 (0)	20 (9.6)
diabetics	0 (0)	3 (6.8)	0	3 (6.2)	0	3 (4.6)	0	3 (4.3)
PAD	1 (4.5)	4 (11.4)	1 (5.9)	4 (10.0)	0	5 (10.0)	0	5 (8.8)
Enterococcus faecalis +								
all wounds	6 (6.7)	7 (5.8)	4 (5.6)	9 (6.4)	5 (22.7)	8 (4.2)*	0	13 (6.2)
diabetics	0 (0)	3 (6.8)	0	3 (6.2)	0	3 (4.6)	0	3 (4.3)
PAD	0 (0)	2 (5.7)	0	2 (5.0)	0	2 (4.0)	0	2 (3.5)
Bacteroides fragilis +								
all wounds	1 (1.1)	3 (2.5)	1 (1.4)	3 (2.1)	1 (4.5)	3 (4.6)	0 (0)	4 (1.9)
diabetics	0	1 (2.3)	0	1 (2.1)	0	1 (1.5)	0	1 (1.4)
PAD	0	1 (2.9)	0	1 (2.5)	0	1 (2.0)	0	1 (1.8)

Because of the small numbers of other micro-organisms in comparison to the presence of Staphylococcus aureus, a semi-quantitative analysis in detail (negative, scant (+/-), low (+), moderate (++), and heavy (+++) was relevant for *Staphylococcus aureus,* but not for the other micro-organisms found. However, no significant correlation between the clinical assessments and the quantitative swab results for *Staphylococcus aureus* (negative, scant (+/-), low (+), moderate (++), and heavy (+++) was found (all Chi square p-value >0.05, *Table 5*).

Table 5: Results of quantitative swab analysis for *Staphylococcus aureus* in relation to the clinical assessment.

Bacteria	Positive clinical symptoms (n, %)	
Staph. aureus	yes	no
nil	51 (47,2)	42 (40,8)
Scant (+/-)	4 (3,7)	1 (1,0)
Low (+)	17 (15,7)	15 (14,6)
Moderate (++)	18 (16,7)	28 (27,2)
Heavy (+++)	18 (16,7)	17 (16,5)

When the clinical assessment of infection was based on one of the highly indicative clinical symptoms, i.e. 'pain/more pain' or 'new pain', or 'delayed (or stalled) healing', no significant correlation between the results of the clinical assessment and the microbiological results of the wound swabs was found (all Chi square p-values >0.05, *Table 4*).

B. Wounds of patients suffering from diabetes mellitus or PAD

Diabetes mellitus:

The same analyses were made for the 69 diabetic wounds as for the total population. Out of 69 wounds, 25 (36%) were clinically assessed as infected, while 59 (86%) had a positive swab result. No significant relationship was found between the clinical assessments and the results of the swab analysis (all Chi square p-value >0.05, *Table 3*). For the group of diabetic patients, no significant relationship was found between the clinical assessments of the wounds and the species of microorganisms or their frequency from the swabs. The same was also true for the indicative symptom 'delayed (or stalled) healing'. Six patients showed the symptom 'pain/more pain', and none of the diabetic patients were clinically assessed to have 'new pain' *(Table 4)*.

Peripheral arterial disease (PAD):

The same analyses were performed for the group of patients suffering from PAD (42 patients, 57 chronic wounds). Out of 57 chronic wounds, 22 (39%) were clinically assessed as infected, and 35 (61%) had a positive swab result. No significant relationship was found between the clinical assessments and the results of the swab (all Chi square p-values >0.05, *Table 3)*. For the wounds of PAD patients, no significant relationship between the clinical assessments and the species of microorganisms or their frequency from the swabs was found. Analysing the indicative symptoms 'delayed (or stalled) healing', 'pain/more pain' and 'new pain', no significant correlation was found with type and frequency of bacterial species *(Table 4)*.

C. Wounds of patients treated with local antiseptics and/or systemic antibiotics

In 143 (68%) of all the 211 chronic wounds, antiseptics and/or antibiotics were used within a period of two weeks before the clinical assessment and swab taking. The antiseptics Edinburgh Solution of Lime (EUSOL-paraffin) and enzyme alginogel were more frequently used than others (n=55, 71%). For two of the wounds, local antibiotics (Fucidin, n=2) were used. For seven wounds (3%), systemic antibiotics were taken orally (i.e. penicillin, n=2; macrolide, n=1; quinolone, n=1; 'others', n=3).

D. Wounds of patients not treated with local antiseptics and/or systemic antibiotics

In 68 (32%) of the 211 wounds, no antimicrobials were used within a period of two weeks before the clinical assessment. Of these 68 wounds, 34 (50.0%) were clinically assessed as infected, while 58 had a positive swab result. No significant relationship was found between the clinical assessments of the chronic wounds and the results of the swabs (all Chi square p-values >0.05, *Table 3)*.

Discussion

The results of this study show that the clinical assessment of infected chronic wounds is not significantly related to the microbiological results of cultures taken by a swab. The analyses performed for patients with a known diagnosis of diabetes mellitus or PAD showed the same results. In this study, 211 chronic wounds in 192 unique patients were systematically analysed. A standardised protocol based on the Levine method for swab taking was used to ensure the swabs were taken in a consistent manner and to minimise variation among healthcare professionals.[29] After sampling, the swabs were transported, processed and analysed within 24 hours at the same microbiological laboratory.[14,26,28,29]

To enhance the reliability of the clinical assessments, the assessing healthcare professionals were specifically educated and provided with example photographs of the diagnostic signs and symptoms.[30] They were also supervised by the first author, who is a physician with a Master of Science in Wound Healing and Tissue Repair. In 68% of the wounds in this study, local antiseptics and/or systemic antibiotics were used as part of the treatment plan within a two-week period before the wounds were analysed. The clinical assessments depended on criteria with limited validation, and swabs were used for microbiological analysis instead of using biopsies or even more modern molecular techniques. In the literature, only one study was found which compared clinical observations with the results of microbiological analyses from wound swabs. In assessing 278 locally infected leg ulcers, Miller et al. also did not find a significant relationship between the clinical assessments and the microbiological analyses.[31]

In this study, swabs were taken using the Levine technique, which is commonly regarded as the best, most practical, reliable and valuable method, as well as the least time consuming and most cost-effective method to microbiologically analyse chronic wounds.[15,32-36] However, some authors have argued that wound swabs may not capture bacteria protected within a biofilm.[27,37] James concluded that 60% of chronic wound specimens originating from diabetic foot ulcers, pressure ulcers and venous leg ulcers, were characterised as containing a biofilm, whereas only 6% of acute wounds were characterised as containing a biofilm.[38]

More recently, it has been argued that up to 90% of chronic wounds have a biofilm.[39,40] The presence of a biofilm in the wounds included in this study may have been a reason for not finding a significant relationship between the clinical assessments and the swab results.[41] Unfortunately, the significant correlation found between the clinical assessment 'no new pain' and no pain/more pain' and the semi-quantitative results for the species *Pseudomonas aeruginosa* and *Enterococcus faecalis* (Chi square, *=p-values <0.05, *Table 4)* depends on too small numbers to be practically significant.

For quantitative culturing of a chronic wound, a biopsy is still considered to be the gold standard.[28,32,42,43] But it is an invasive method of sample collection, and because of the expertise needed and the time requirements for processing, it is not feasible to use biopsies in daily practice. Moreover, Serena et al. did not find a significant relationship between the clinical assessments of chronic venous leg ulcers and the results of cultures taken by biopsy.[44] However, pathogens can also be detected using molecular microbial diagnostic approaches such as polymerase chain reaction (PCR) and 16S ribosomal probes. But these techniques, although more sensitive to detecting bacteria than swab taking, cannot differentiate between viable and nonviable bacteria, and the short read lengths that are generated are often insufficient to provide species-level discrimination.[45-48]

In this study, the clinical assessments were based on several signs and symptoms described by the WUWHS. Although they were based on previously published literature and expert opinions, no validation studies on these criteria are known.[9,49] The percentages of bacterial species found by semi-quantitative analysis are in line with previous results,[17,53,54] although Bowler isolated more anaerobes (36% of isolates compared to 2% in this study), i.e. *Peptostreptococcus spp. and Bacteroides spp*.[54] Although specimen collection and transport were performed with the utmost care, securing the swabs at 4˚C in the Amies gel transport medium may have led to increased oxygen diffusion and unintended selective death of the anaerobe bacteria.[55] Because no significant relationship was found between the clinical assessments and the microbiological results of cultures taken by a swab in the sample as a whole, it was not strange to find no significant relationship in the wounds of patients suffering from diabetes or PAD, because the chronic wounds of these patients are more difficult to assess clinically. The main limitation of this study is the frequent use of local antiseptics and systemic antibiotics, which possibly influenced the results of this study. However, the results of the remaining 68 wounds, those not affected by the use of antiseptics and/or systemic antibiotics, (32%, *Table 3*), did not differ from the results of the study sample as a whole.

From this study, it can be concluded that the result of a swab analysis does not support the clinical assessment of a chronic wound. Standard clinical microbiological tests may culture planktonic bacteria, but probably do not adequately measure biofilm bacteria.[41] Although new molecular biological technologies seem promising, they are not yet feasible for use in daily practice. Therefore, for the time being, it is preferable to assess chronic wound infection clinically. For a better clinical assessment of the bacterial burden in the presence of a biofilm, studies validating the signs and symptoms of chronic wound infection are needed.

Conclusion and recommendations

This study proves that microbiological analysis of chronic wounds to support the clinical assessment is waste of time. New molecular microbiological technologies are not yet ready for practical use, so it is preferable to assess chronic wounds clinically. However, studies validating the diagnostic signs and symptoms of chronic wound infection are needed.

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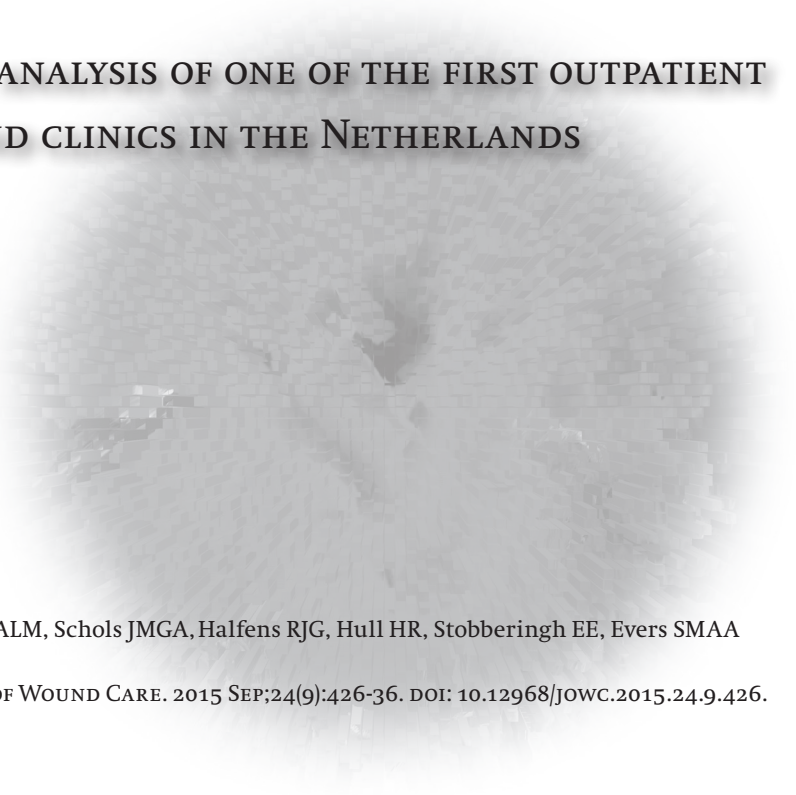
Chapter 6

Cost analysis of one of the first outpatient wound clinics in the Netherlands



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Abstract

Objective
To perform, from an insurance perspective, a cost analysis of one of the first outpatient community wound care clinics in the Netherlands, the Knowledge Centre in Wound Care (KCWC) at Venray.

Methods
This study involved a cost analysis based on an observational cohort study with a one-year pre-admission and a one-year post-admission comparison of costs. Patients were included when they first consulted the outpatient wound care clinic. Participants were all insured by the same health insurance company, Coöperatie Volksgezondheidszorg (VGZ). A standard six-step procedure for performing cost studies was used to calculate the costs. Given the skewed cost data, non-parametric bootstrapping was used to test for statistical differences.

Results
172 patients were included in this study. The difference in costs related to wound care between the year before and the year after initial admission to the wound clinic resulted in a reduction of € 2,533 per patient in the base case analysis. The categories 'general practitioner', 'hospital care', 'mental health care' and 'transport' scored lower, indicating lower costs, in the year after admission to the wound clinic.

Discussion
In this study, only the reimbursement data of patients of one health insurance company, and specifically only those made under the Health Insurance Act, were available. Because of the observational design, definitive conclusions cannot be made regarding a demonstrated reduction of costs in the year post-admission. Nevertheless, this study is a first attempt of a cost analysis of an equipped outpatient wound clinic as an innovative way of responding to the increasing number of chronic wounds in the Netherlands. The calculations show that savings in wound care are possible.

Declaration of interest
A possible conflict of interest should be mentioned. First author AALM Rondas, PhD student at Maastricht University, is working at the KCWC wound clinic at Venray in the Netherlands as a physician. However, the research data were provided externally by Coöperatie Volksgezondheidszorg (VGZ) and checked by the academic co-authors, none of whom have a conflict of interest. The authors have no financial or commercial interest to declare.

Introduction

At any given time, almost 1% of the world's population experiences chronic wounds, with associated costs accounting for more than 2–4% of health care expenses worldwide.[1] Within the next 40 years, the cost burden of treating chronic wounds is expected to grow rapidly due to the aging population and a sharp rise in the incidences of diabetes and obesity worldwide.[2-5] The National Health Service in the United Kingdom has estimated the costs of chronic wounds to be € 38–59 per inhabitant (€ 2,34–3,51 billion in total) per year.[6] In the United States, chronic wounds caused by pressure, venous stasis or diabetes mellitus affect 6,5 million patients (2% of the total population) each year and are estimated to cost in excess of € 61 per year per resident (€ 19 billion in total).[5,7]

A cutaneous wound is a break in the continuity of tissue structure and can be described in terms of erosion, ulcer or fissure.[8] When wounds do not proceed through the healing process in an orderly and timely enough manner to achieve anatomic and functional integrity, they are considered to be chronic wounds.[9] Chronic wounds are often painful and debilitating, resulting in an extreme diminishing of quality of life.[10-12] The costs for the treatment of chronic wounds are partially due to wound complications that require hospitalisation or cause a delay in hospital discharge.[13-16] However, many of these costs seem avoidable, since admission is only necessary for those patients requiring intravenous therapy or a surgical intervention.[13,17]

In the 1990s, this was the main reason for the United Kingdom to advocate for the benefits of specialised leg ulcer clinics and to set up community-based wound management clinics.[18] Since then, these clinics have provided comprehensive wound care. Home care nurses were trained and guided by nursing specialists in vascular surgical service and were made responsible for the daily running of and ordering for the clinic. The vascular status of the patients was structurally assessed by measuring their Ankle Brachial Pressure Index (ABPI). When applicable, compression bandages were changed in the clinic at least once a week. These clinics provided patients with easy access to care.

Several authors have shown that wound care programmes that are planned, coordinated and operate using evidence-based guidelines can reduce costs substantially, while improving healing rates.[1,19-21] The combination of nursing skills, the structural clinical assessment of patients and the accessibility of equipment (Doppler probe, bandages and stockings) in the community clinics lead to an overall faster healing rate for leg ulcers, with a 12-week healing rate of almost 70%, compared with 22% before these leg ulcer clinics were set up.[18,20,22,23] Treatment in leg ulcer clinics has likely been more cost effective than treatment in the existing hospital-based wound care clinics[19,23-25] and has had a positive impact on several indicators of patients' quality of life.[1,18,26,27]

As in the UK previously,[28] the treatment of chronic wounds in the Netherlands is still rather fragmented, ineffective and done with inadequate professional standardisation. Patients may receive treatment in a scattered landscape of intra- and extramural working health care professionals, such as family doctors, medical specialists, elderly care specialists, physician assistants, nursing specialists, district nurses, paramedics, occupational therapists, podiatrists and dieticians. Expensive dressings are used by a variety of wound care professionals and not always in the most comprehensive way.[29,30]

Because of this, van Mierlo-van den Broek recommended the innovative organising of chronic wound care in the Netherlands. In her opinion, a quick referral to genuine wound care specialists is prognostic of a positive chronic wound outcome.[29] Financial constraints have led to increasing recognition of costs. Wound care products form a major subsector, and along with staff costs, constitute a major cost burden for healthcare providers. It is therefore understandable that development of new, 'advanced', and more effective medical devices aimed at improved wound care provision is desirable but must be achieved within the constraints of cost effectiveness.[31-36]

With the aim of achieving effective and efficient care for patients suffering from chronic wounds, in 2009 a community-based outpatient wound care clinic was opened in the South of the Netherlands. The Knowledge Centre in Wound Care (KCWC) at Venray is one of the first of its kind in the Netherlands. Unlike the community-based clinics in the UK, the KCWC accepts all kinds of chronic wounds. At the start of the wound clinic, two nurses were specifically educated in chronic wound care and were supervised by an elderly care physician with a postgraduate degree in wound healing and tissue repair.

For the most part, patients of the wound clinic are referred by their general practitioner (GP). They are asked to take their medical record and health insurance information with them to their first appointment at the wound clinic. During the intake, patients are seen by one of the nurses together with the wound clinic physician. This combination of professional expertise is useful in indicating the underlying diagnosis of the wound, in evaluating the patient's wound and in formulating a tailor-made treatment plan. In the case of a leg ulcer, additional assessment is done, and occasionally patients are referred to other specialists such as a podiatrist, occupational worker or an orthopaedic shoemaker. Their professional contributions are part of patients' integral treatment plans and are guided by the designated case manager from the wound clinic. Patient follow-up is conducted during regular appointments at the wound clinic, together with home care nurses who strictly execute the wound treatment plan.

The economic and effectiveness evidence of wound care community clinics in the UK[19, 23-25] encouraged us to perform a cost analysis of one of the first outpatient community wound care clinics in the Netherlands (KCWC). In order to perform a cost analysis, it is necessary to determine the resources used and their costs. In this study, the database consisting of the reimbursement costs of patients insured by Coöperatie Volksgezondheidszorg (VGZ) has been used.

The research question of this study is as follows: From an insurance perspective, is there a difference in healthcare costs (specifically, costs that qualify for reimbursement under the Health Insurance Act) in the year before a patient's first visit to the KCWC and the year following a patient's first visit to the KCWC?

Method

Design

The study involved an observational cohort study with a pre- and post-comparison. For the cost analysis, the reimbursement data from the health insurance company VGZ are used, which more specifically includes only costs that qualify for reimbursement under the Dutch Health Insurance Act.

Health insurers in the Netherlands each have a certain regional distribution. VGZ is the main health insurance company in the Northern Limburg region, in which the KCWC is active. The company has an 80% coverage rate in the region, providing coverage for about 300,000 inhabitants.

Dutch health insurance system

The Dutch health insurance system is comprised of three compartments, divided by three laws: the Health Insurance Act (Zvw), the Exceptional Medical Expenses Act (AWBZ) and the Social Support Act (Wmo). The first compartment consists of the obligatory basic insurance for essential curative care pursuant to the Health Insurance Act (Zvw), related to care by a GP or hospital care, for instance. The second compartment, organised under the Exceptional Medical Expenses Act (AWBZ), consists of an obligatory national insurance for long-term and unaffordable care, e.g. home care and long-term institutional care for the elderly and the chronically ill. Since 2007, domestic (household) care has been arranged under the Social Support Act (Wmo).

Everyone in the Netherlands is required to have basic health insurance (first compartment). The Health Insurance Act establishes which provisions are incorporated into the basic package, which is the same for each insurer and is determined by the government.[37] Insurance companies can also offer supplementary voluntary insurance for forms of care deemed less essential. In this study, only the costs that qualify for reimbursement under the Health Insurance Act (Zvw) were used. During the study period, the costs that qualify for reimbursement under the Exceptional Medical Expenses Act were not available, and therefore could not be included in our analysis.

Inclusion and exclusion criteria

Patients insured by VGZ who had their initial consultation with the outpatient wound care clinic from 15 September 2009 through 15 September 2010 were included in this analysis. The costs were calculated from the year before their initial consultation to the year following their initial consultation. Reimbursement data therefore includes the period from 15 September 2008, i.e. first pre-measurement for the first patient included in the study, until 15 September 2011, i.e. the final post-measurement of the last patient included in the study. The latter date is chosen because insurance reimbursements could take a time lag of two years to be processed, making a later time frame (until 2014) unfeasible. Only patients insured by VGZ were included, as the company was the exclusive source for deriving the wound care costs.

Setting and procedure

In this study, nearly all patients (97%) were referred to the KCWC by their general practitioner, leaving a few patients who were referred by a medical specialist. During their treatment, patients visited the wound clinic frequently, at least once a week. When they were not physically capable of visiting the outpatient clinic, they were treated at home.

During the intake, all patients were assessed to diagnose their wound. Treatment was managed according to an evidence-based protocol, using Tissue Infection Moisture and Edge (TIME) principles.[38-42] After each consultation, patients were provided with enough wound dressings to last until their next planned appointment. In between visits at the clinic, home care nurses were structurally involved and executed the treatment plan as prescribed, operating under the responsibility of the wound clinic.

During their first consultation at the wound clinic, patients were asked for the date of the first occurrence of their wound. The exact date was verified by looking into the medical record provided by each patient's GP, and the written medical correspondence between the GP and the hospital specialists involved in their wound treatment. The cause of the existing wound was diagnosed by exploring the written medical correspondence between physicians and/or by an additional clinical assessment of the patient at the clinic. All leg ulcers were additionally assessed by determining the patient's Ankle Brachial Pressure Index (ABPI).[43-48] The ABPI indicated whether the leg ulcer was of venous (ABPI >0.8), mixed (ABPI 0.6-0.8) or arterial (ABPI <0.6) origin.

Ethical consideration

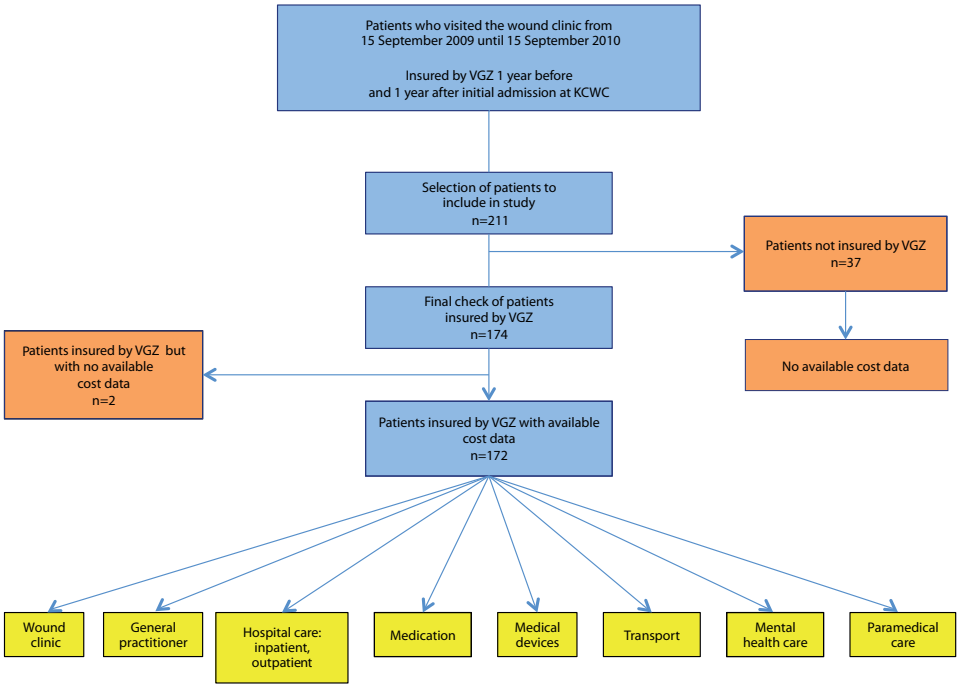
Prior to the execution of the study, patients were informed of the methodology and were asked for their permission to use their insurance claim data and medical records for the purpose of this study. Because patients were not subjected to acts and/or specific behaviors, the study did not fall under the Dutch Medical Research Involving Human Subjects Act (WMO). Therefore, there was no legal need for the study to be evaluated by a medical ethics committee.[49]

Given the surname of each participant and his/her date of birth, VGZ used the unique personal Dutch social security number (BSN) to gather the reimbursement costs per patient. The researcher and VGZ's data analyst combined patients' BSNs and their reimbursement costs. In the mutual communication between the researcher and the data analyst, the anonymity and privacy of the participants were maintained, and any personal data was kept confidential.

Cost calculation

Cost calculations were performed according to the existing international standards.[50,52] According to these standards, a six-step procedure for performing costing studies is included.[50,51] The first step involves determining the scope of the study and takes the perspective and the time period into account. The costing in this study was performed from a health insurance perspective, relative to the Zvw. The time horizon for measuring costs was one year, i.e. one year before and one year after a patient's initial consultation at the wound clinic. Using this time horizon, the patient group was able to be its own control *(Figure 1)*.

Figure 1: Inclusion and exclusion of patients and measured cost categories per patient 1 year before and 1 year after initial wound clinic admission.



The second step concerns the choice of cost categories that are measured.[50,51] This study measured 'healthcare sector costs' related to prevention, diagnosis and treatment of chronic wounds, as well as 'patient and family' costs, i.e. the costs of medical transport to and from the wound clinic, by taxi (with wheel chair provisions) or by ambulance, which fall under the Health Insurance Act.[53,54] The costs included in our study are: contacts with health care professionals (general practitioners, medical specialists, paramedics, mental health professionals), medication, medical devices and hospitalisation. Considering the content of their professional work in relation to wound care, surgeons, plastic surgeons and dermatologists were looked at as relevant subgroups of medical specialists, as were physiotherapists, occupational therapists, dieticians and paramedics. From the category of medical devices, the costs for wound dressings were taken separately.

The third step was to determine the resources to include in the cost analysis. A data analyst (H.H.) employed by VGZ explored the VGZ database of expenses claims as the primary resource for this study. In the fourth step, the volume of resources was measured. The fifth step involved the valuation of the resources used, and the sixth step was calculating the unit costs for each patient by multiplying the volumes of the resources used by the unit prices. The VGZ database consisted of both the expenses claims of health care providers and the claims submitted by patients themselves. For the measurement and evaluation, the VGZ database was used (i.e. the 4th, 5th and 6th steps were provided by VGZ), wherein the total costs per resource and per patient were given in one table.

Bootstrap resampling method

The distribution of cost data is usually skewed. It is difficult therefore to provide a valid comparison and inference regarding the differences in the arithmetic means of costs between the years before and after the admission of patients to the wound clinic. Therefore, non-parametric bootstrapping has been used to test for statistical differences between the periods of one year before and one year after admission to the wound clinic.[55] Non-parametric bootstrapping is a method based on random sampling, with replacement based on patients' individual data.[56] It is a way of finding the sampling distribution from only one sample.[57] Estimates (such as mean, standard deviation and confidence interval) are extracted from a non-parametric data set (no underlying distribution is assumed in the data set) to provide an approximation of the accuracy of the statistical estimates.[53,54] This represents the uncertainty in the costs and tests whether there are significant differences between the costs of both periods.[58] In this study, the non-parametric bootstrap resampling method has been applied with 1,000 replications. Using these 1,000 bootstrap replications, the 95% confidence intervals around the costs were calculated, based on the 2.5th and 97.5th percentiles. The data on the health care costs were analysed using the Microsoft Excel bootstrapping tool.

Base case analysis

The base case refers to the most probable estimation of the case in which the reimbursement costs of 172 patients were included. In this analysis, the visits of patients at the wound clinic were calculated as intervention costs. Because the patient data on expenses for home care (under the Exceptional Medical Expenses Act) were not available, the most likely frequency of home care nurses visits was estimated at five home care visits per week per patient. This estimate was influenced by the frequent prescription of Edinburgh Solution of Lime (EUSOL-paraffin), which always required the application of EUSOL-paraffin twice a day.

Sensitivity and subgroup analysis

To determine the likely impact of using an alternative value of variables, three sensitivity analyses and a subgroup analysis were performed.

A. Frequency of home care visits for wound dressings changes

In a first sensitivity analysis, the influence of (minimum and maximum) intervention costs was analysed. Intervention costs per patient were calculated using the sum of costs of visits at the wound clinic together with the costs of home care visits for dressing changes. The minimum of one home care nurse visit versus the explicit maximum of thirteen visits per week were counted. The same patient visited the wound clinic once a week.

B. Duration of wounds

The second sensitivity analysis was meant to show the influence of the duration of the existence of patients' wounds on the outcome of costs. Therefore, the group of 172 patients was divided in two groups by their computed median of wound duration and for each group (less or more than 75 days), a cost analysis was made.

C. Expensive wound dressings

In a third sensitivity analysis, the impact on the outcome of patients having abnormally high reimbursement costs of wound dressings was computed. The patient costs of more than € 5,000 after admission were replaced by the computed median of dressings costs for the whole group of 172 patients. In a last sensitivity analysis, patients whose dressings cost more than € 5000 after admission were left out of the calculation.

D. Subgroup analysis

This analysis had the specific intention of determining whether there were differences in reimbursement costs per patient and per wound type, between the year before and the year after patients were admitted to the wound clinic. Because they represented together more than two-thirds of all wounds (i.e. 116 out of 172 chronic wounds, or 67%), a subgroup analysis of reimbursement costs for the diagnoses 'leg ulcers', 'pressure ulcers' and 'diabetic ulcers' was done.

Results

Inclusion

From 15 September 2009 through 15 September 2010, 211 outpatients visited the wound clinic for the first time. 174 of them were insured by VGZ, whereas 37 (21.3%) patients were otherwise insured, and were excluded from this study *(Figure 1)*.

Table 1. Baseline characteristics of included patients (n=172) and the median duration of wound treatment (days) per diagnosis.

Female (%)	**66.7**	**Median duration of treatment (days)**
Age (mean in years, SD)	**66 (1.41)**	
Diagnosis (n, %)		
· venous leg ulcers	54 (31)	101
· arterial leg ulcers	20 (12)	92
· mixed leg ulcers	5 (3)	52
· pressure ulcers	32 (19)	37
· diabetic ulcers	15 (9)	50
· post-traumatic	14 (8)	177
· post-surgical	10 (6)	74
· oncologic	9 (5)	94
· dermatomycosis	5 (3)	45
· burns	2 (1)	23.5
· others	6 (4)	76
Total	**172 (100)**	**2,509**

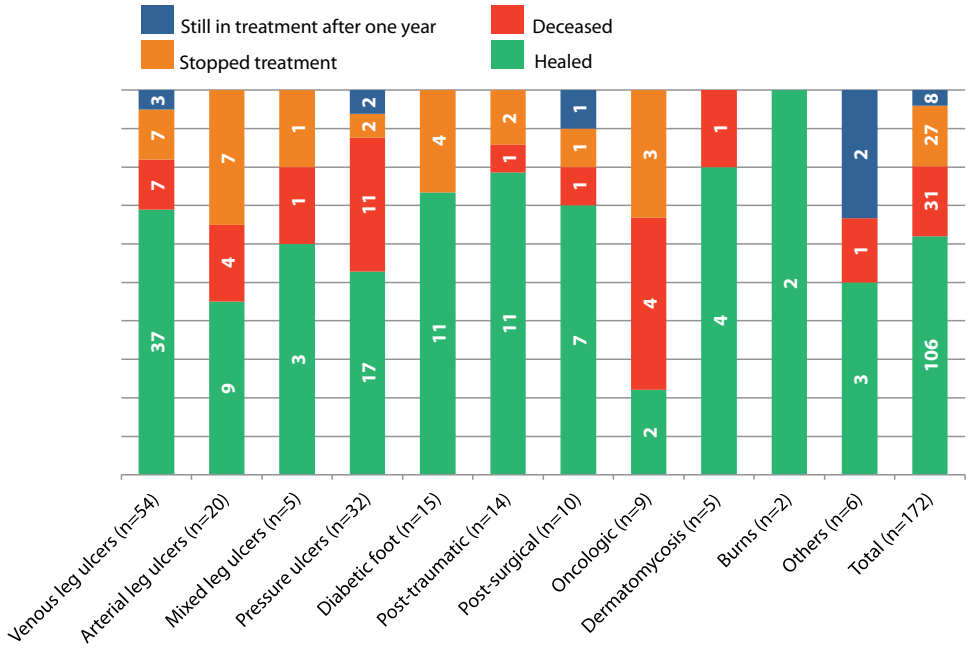
Characteristics of patients and wounds

The age of the patients varied from 3 to 94 years of age (mean: 66, SD: 1.41); 66.7% of patients were female *(Table 1)*. Venous leg ulcers, pressure ulcers and arterial ulcers were the most common types of complex wounds, and were represented with respectively 54 (31%), 32 (19%) and 20 (12%) *(Table 1)*. The category 'others' (n=6) was comprised of wounds of different aetiology: skin tears, a wound at the entrance of an urostoma incontinence associated dermatitis, a peri-anal ulcer, a leg ulcer as a consequence of a complex regional pain syndrome type 1 (CPRS) and a leg ulceration having congenital lymphoedema as etiological factors *(Table 1)*. The median durations of existence of the venous, arterial and mixed ulcers were respectively 101, 92 and 52 days, whereas diabetic ulcers had a median duration of 50 days, and post-traumatic wounds of 177 days *(Table 1)*.

During treatment at the wound clinic, 106 patients (62%) completely healed, and 8 patients (4%) were still in treatment after one year. After their initial admission, 27 patients (16%) discontinued treatment at the wound clinic. Of these, 18 were referred to the hospital (8 to the vascular surgeon), and 1 patient who was being treated at the wound clinic and hospital simultaneously chose to stop treatment at the wound clinic and only be treated further at the hospital.

Because of their experience with the prescribed sharp debridement and/or ambulant compression therapy, 8 patients discontinued their treatment at the wound clinic. The treatment outcomes of these 27 patients after their discharge from the wound clinic is unknown. Thirty-one of the included 172 patients (18%) became deceased, with no derivable relation to the existence of their chronic wound *(Figure 2)*.

Figure 2. Treatment outcomes (in absolute numbers) for wound clinic patients with various types of chronic wounds (n=172).



Results of cost analysis

Base case analysis

Both the arrhythmic and the bootstrapped cost differences between reimbursement costs one year before and one year after admission to the wound clinic are shown in *Table 2*. The arrhythmic median costs are different than and not comparable to the bootstrapped median costs. The total bootstrapped mean costs over the period of one year after initial admission to the wound care clinic amounted to € 20,693 per patient, in comparison to € 23,226 the year before they were admitted. The total bootstrapped mean costs were 9% lower after the admission of patients at the outpatient wound clinic.

Looking at different cost categories, the bootstrapped mean costs per patient per year for patients' contacts with their GPs were higher in the year before admission to the outpatient wound clinic (€ 489) than the year after (€ 380). Also, the expenses of 'hospital care' reduced from € 17,098 to € 11,166 per patient. For all the medical specialist subgroups, the bootstrapped costs were lower in the period after admission at the wound clinic.

The same was true for 'mental health care' and 'transport', whereas the bootstrapped median costs for 'paramedical care' and 'medical devices', including the costs of wound dressings, were higher in the period after admission *(Table 2)*.

Table 2: Base case analysis. Arrhythmic and bootstrapped healthcare costs per patient per subgroup per period.

	Period of a year before admission to the KCWC				Period of a year after admission to the KCWC				95% bootstrapped confidence interval of mean cost difference
	arrhythmic reimbursed costs		bootstrapped reimbursed costs		arrhythmic reimbursed costs		bootstrapped reimbursed costs		
Costs group	mean (*stdev)	median	mean (stdev)	median	mean (stdev)	median	mean (stdev)	median	
General practitioner	487 (393)	396	488 (30)	489	382 (306)	293	380 (23)	380	-108 (-180,-34)
Medication	1663 (2006)	1128	1661 (155)	1655	1491 (2014)	820	1492 (156)	1485	-169 (-607,246)
Hospital care	17139 (28991)	4375	17219 (2288)	17098	11341 (20726)	3753	11268 (1515)	11166	-5950 (-11461, -650)
• general surgery	3739 (10501)	0	3751 (774)	3692	2663 (9274)	0	2646 (706)	2618	-1105 (-3125, 940)
• plastic surgery	178 (1157)	0	174 (89)	163	153 (1407)	0	149 (108)	129	-25 (-275,272)
• dermatology	321 (906)	0	316 (69)	309	336 (1946)	0	340 (147)	324	24 (-244,376)
Paramedical care	554 (1173)	84	549 (95)	541	602 (1435)	76	601 (108)	598	53 (-238, 334)
• physiotherapy	519 (1144)	31	517 (85)	511	525 (1382)	0	519 (104)	510	0 (-260, 281)
• occupational therapy	19 (73)	0	19 (5)	19	42 (157)	0	42 (12)	41	22 (-1,51)
• dietician	14 (45)	0	14 (3)	14	22 (64)	0	22 (5)	21	8 (-4,19)
Medical devices	1908 (3897)	791	1920 (302)	1897	2726 (6673)	858	2742 (505)	2719	822 (-226,2071)
• dressings	854 (3072)	189	849 (235)	818	1671(6127)	337	1689 (465)	1637	846 (-106, 2005)
Mental health care	63 (395)	0	64 (31)	60	23 (129)	0	23 (10)	22	-41 (-112, 14)
Transport	614(1366)	0	615 (104)	611	477 (1316)	0	478 (99)	474	-138 (-427, 149)
Wound clinic	--	--	--		1998 (2112)	1303	1991 (157)	1984	--
TOTAL costs	**23283 (32441)**	**10940**	**23226 (2469)**	**23238**	**18712 (25911)**	**8777**	**20693 (1973)**	**20612**	**-2533 (-8916, 3489)**

*sdev: standard deviation

Sensitivity analysis

A. Frequency of home care visits for changing wound dressings

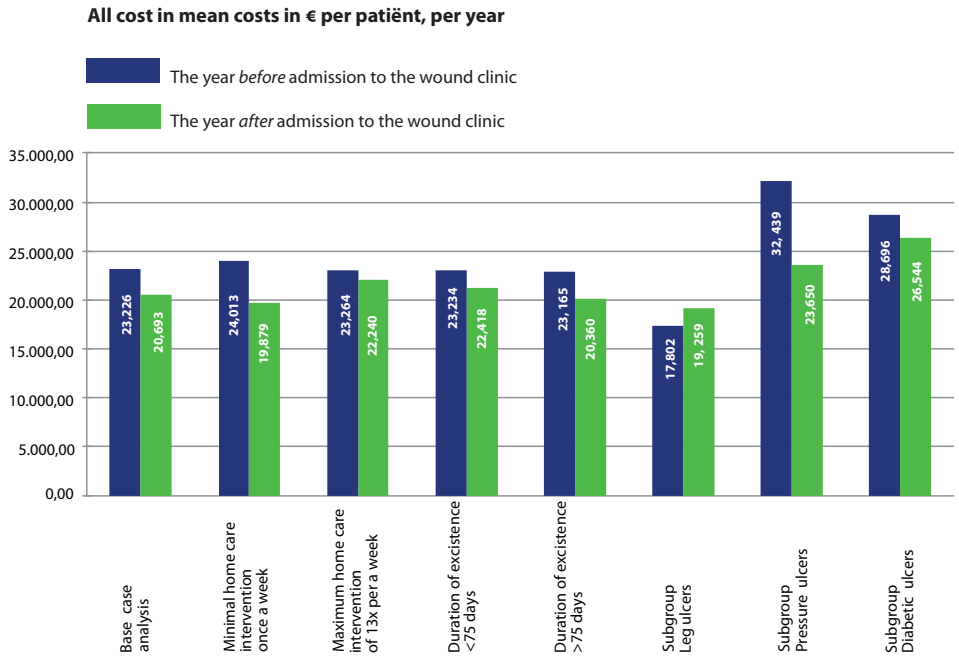
For the base case analysis, the assumption of six appointments per week per patient was made: five visits by a home care nurse and one outpatient visit at the wound clinic. *Figure 3* shows the difference in the outcome of bootstrapped costs when counting the minimum of 1 home care visit per week versus the maximum of 13 home care visits. When focusing on the minimum intervention of home care and calculating the mean of the cost difference between the year before and after visiting the wound clinic of the true population was € 4,134 per patient. It was 95% confident that the true population median of the cost difference was between € 10,198 and € 1,764 per patient *(Figure 3)*. For the maximum intervention of home care, the median of the cost difference was € 1,025 per patient per year (95% confidence interval: € 7,692 to € 5,172 per patient, (*Figure 3)*.

B. Duration of wounds

Dividing the group of 172 included patients by the computed median wound duration of 75 days, a difference in the outcome of costs between the two groups was calculated. For wounds that had a duration of more than 75 days, the computed mean of cost difference of the true population was €2,805 per patient per year (95% confidence interval: -€ 11,410 and € 5,945 per patient, *(Figure 3)*.

For wounds with duration of less than 75 days, the mean of the cost difference of the true population was € 1,816 per patient. (95% confidence interval: -€ 10,973 to € 6,661 per patient *(Figure 3)*.

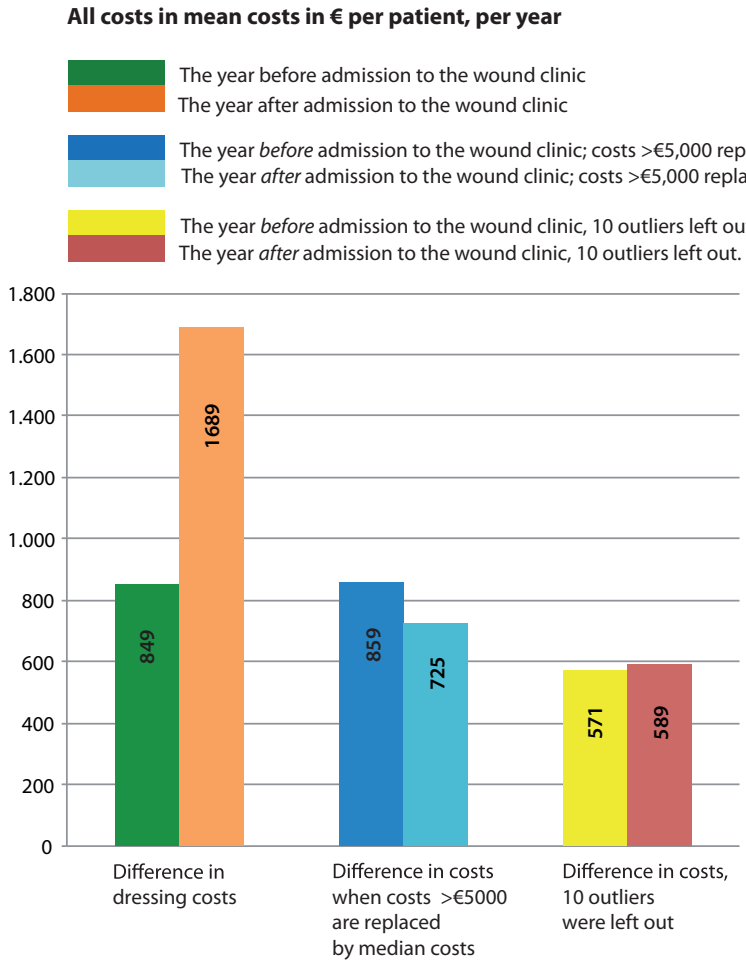
Figure 3: Differences in costs between the year before and after patients admission to the wound clinic: base case analysis (columns 1-2), sensitivity analysis (columns 3-10) and subgroup analysis (columns 12-16).



C. Expensive wound dressings

When in the sensitivity analysis for those patients whose dressings cost more than € 5,000 (n=10), the reimbursement costs were replaced by the median (€ 1,689) of the included group of 172 patients, the mean bootstrapped costs of dressings were lower in the year after patients' first visits to the wound clinic. It was computed that the mean of the cost difference of the true population was € 134 (95% confidence interval: -€ 737 and € 250 per patient, *Figure 4*).

Figure 4. Comparison of reimbursement costs of dressings before and after admission; costs when patients with significantly expensive dressing costs were replaced by median costs.



When the patients whose dressing cost more than € 5000 (n=10), were left out of the calculation in a sensitivity analysis, the mean bootstrapped costs of dressings were higher in the year after patients' first visit to the wound clinic. It was computed that the mean of the cost difference of the true population was € -18 (95% confidence interval: -€ 215 to € 240 per patient, *(Figure 4)*. This group of 10 'outlier' patients with extraordinary expenses together constituted 81% of all costs of dressings (€ 227,296) after admission to the wound clinic. Before admission, these 10 patients constituted together 35% of dressing reimbursement costs *(Figure 4)*. Out of these 10 patients, 4 suffered a venous leg ulcer, 1 of them complicated by an underlying lymphedema; 2 patients suffered pressure ulcers, both as a consequence of an existing paraplegia; 1 patient had an inoperable skin tumor at the back of her head; and 1 had a post-operative 'platschbauch' for more than a year before visiting the wound clinic.

Within 2 weeks after their admission, 2 of these 10 patients whose reimbursement costs for dressings exceeded € 5,000 (suffering a diabetic foot ulcer and a venous leg ulcer) left the wound clinic of their own choice for further treatment in the nearby hospital. Those two patients alone constituted together more than 35% (€ 82,656) of the wound dressing costs of the group of patients the year after their initial visit to the wound clinic.

D. Subgroup analysis

For leg ulcers, pressure ulcers and diabetic ulcers, a separate subgroup analysis was done. It showed that for pressure ulcers (n=32) the mean of the cost difference of the true population was € 8,789 (95% confidence interval: -€ 19,333 to € 2,212 per patient, *Figure 3*). For diabetic ulcers (n=15), the mean of the cost difference between the two periods of time of the true population was € 2,152 (95% confidence interval: -€ 10,683 and € 7,228 per patient, *Figure 3*).

Those two groups contrasted with the computed mean of the cost difference of the leg ulcers (n=79), which was -€1,458 per patient (95% confidence interval: -€ 7,645 and € 9,533 per patient, *Figure 3*). The bootstrapped costs of the leg ulcer patients were higher per patient the year after admission than the year before *(Figure 3)*.

Discussion

This study is the first cost analysis of an outpatient community wound care clinic in the Netherlands. It showed that the way wound care for chronic wounds in such a clinic is offered, may be therapeutically effective (complete healing was achieved in 106 patients, 62% of included patients) and that it resulted in a cost reduction in the year after admission for most wound types as well, but not for leg ulcers. The percentage of patients with complete wound healing (62%) was comparable to that of other wound clinics in the UK,[22,23] though patients in the KCWC clinic have many kinds of chronic wounds and not only venous leg ulcers.

The pre-and post-admission comparison in the base case analysis showed that considerable savings in reimbursement costs (€2,533 per patient per year) were achieved. After the initial admission of patients, the categories 'general practitioner', 'hospital care', 'mental health care' and 'transport', scored lower in reimbursement costs, whereas 'paramedical care' and 'medical devices' (including wound dressings) scored higher. The multidisciplinary character of wound treatment may well explain the additional expenditures for 'paramedical care' and 'medical devices' the year post-admission. In addition to wound care, the wound clinic may arrange a nutrition plan, elastic stockings, orthopaedic shoes, and also pressure-reducing cushions and mattresses for (predictive) pressure ulcer patients. Therefore, different specialists were often involved, such as a dietician, an orthopaedic shoemaker and an occupational therapist.

Some health economists argue that in wound care, most of the expenses are made by hospitalisation or delayed hospital discharge, followed by nursing time and dressings.[14,15] In this study, the year before the first visit to the wound clinic, 'hospital care' constituted 74% of the costs, whereas the year after admission 'hospital care' expenses were less, constituting 54% of the costs.

In our analyses, the data of the intervention costs of the home visits by a nurse were not available, as these are not covered by the Health Insurance Act. In the base-case analysis, we assumed 5 visits per week from a home care nurse. A sensitivity analysis showed the influence of the frequency of home care visits on the cost difference between the year pre- and post-admission at the wound clinic. Even when the home care visits were calculated at the maximum of 13 times per week (along with 1 visit to the wound care clinic, i.e. max. 14 dressing changes per patient, per week), costs were still less post-admission, indicating that the cost saving is not significantly influenced by the assumption of 6 visits (5 home and 1 clinic) per week. In reality, the decrease in costs may be even greater than calculated, as patients also may have received home care before their first visit to the wound clinic, while we assumed that the costs for home visits in the year before admission to the clinic were zero.

Additionally, the sensitivity analysis showed the robustness of our analysis. For wounds that existed longer than 75 days, the cost reduction is higher than for those lasting a shorter amount of time. Literature shows that wounds of longer duration may benefit from an early and aggressive treatment, as they are associated with excessive inflammation, fibroblast senescence, and alterations in wound bed flora.[59]

Chronic wounds that exist longer than 75 days benefit more from treatment at the wound clinic, than those that exist for a shorter amount of time.

The subgroup analysis shows a reduction in costs post-admission for pressure ulcers and diabetic ulcers, but not for leg ulcers. The calculated annual costs of treating a leg ulcer per patient in this study are higher than those calculated in the UK, US and Sweden.[60] A diabetic ulcer in this study cost significantly more than a diabetic ulcer in the Prompers study.[61] But differences in the choice of study population, categories and resources make comparisons between cost studies difficult.

Although the reimbursement costs for wound dressings were higher the year post-admission, they were far less than the 20% of costs stated in the literature.[14,15] During the year pre-admission, they constituted 2.7% of all costs, and during the year post-admission they constituted 8.2% of all costs. A great deal of these expenses was related to 10 patients. Of these, 2 discontinued the treatment at the wound clinic within 2 weeks of their initial intake, and were then treated at the hospital. These 2 patients together were responsible for more than 35% of total dressing expenses in the year after their initial admission to the clinic.

This study has several limitations. First, it involves an analysis of just one outpatient wound clinic, in one specific region in the Netherlands by using reimbursement costs of one health insurance company, VGZ. Although VGZ indicated that all incoming expense claims of health care providers and patients were checked, double-checked and approved by their accountants, the study is limited by the exclusive use of the database of one insurance company, which does not register the volume and price of resources separately for each patient and for the period of a year.

Another limitation of this study was the inability to include cost related data other than what fell under the Health Insurance Act (Zvw). Insurance companies in the Netherlands are not allowed to merge files of the Exceptional Medical Expenses Act (AWBZ) and the Health Insurance Act (Zvw) due to ethical concerns. In addition, all home care reimbursement costs related to individual patients that fell under the Exceptional Medical Expenses Act (AWBZ) were not available until 1 January 2012 and could not be included in this study.

Notwithstanding the aforementioned limitations, this study is the first of its kind, which analyses the costs of an outpatient wound clinic in the Netherlands and indicates that such a wound centre is therapeutically effective and cost-saving. A prospective study design, using incident registration for the recording of patient data, wounds and costs, is necessary to be able to draw firm conclusions regarding the effects of the introduction of an outpatient wound clinic on noticeable changes in reimbursement costs. It is also needed to help ensure the further development of effective and efficient outpatient wound clinics in the Netherlands.

Conclusion

Worldwide, a growing number of wound care centres are being established. The emergence of these centres reflects the increasing prevalence of chronic wounds as well as the surmounting cost burden for health care systems. In addition to delivering quality treatment at the wound care clinics, it is essential to establish a financially viable enterprise.[29,62-64] The increase of reimbursement costs related to hospitalisation from chronic wounds has already caused healthcare systems to focus on organising chronic wound care into clinics within the community, with the aim of reducing hospital admissions and re-admissions, as well as facilitating earlier hospital discharge.[62,63,65] This policy also applies to the Netherlands and has resulted in the formation of an outpatient wound clinic in Venray. The Dutch Healthcare Authority has used the evaluation of this and one other initiative in specifically organising chronic wound care in the Netherlands and in advising the Ministry of Health, Welfare and Sport on how to arrange and finance chronic wound care from 2015 onwards.[66]

The set up of the Knowledge Centre of Wound Care in the Netherlands has resulted in complete healing in almost two-thirds of treated patients (62%). The cost analysis that was carried out shows that considerable savings are possible. Further research with a more prospective design is recommended.

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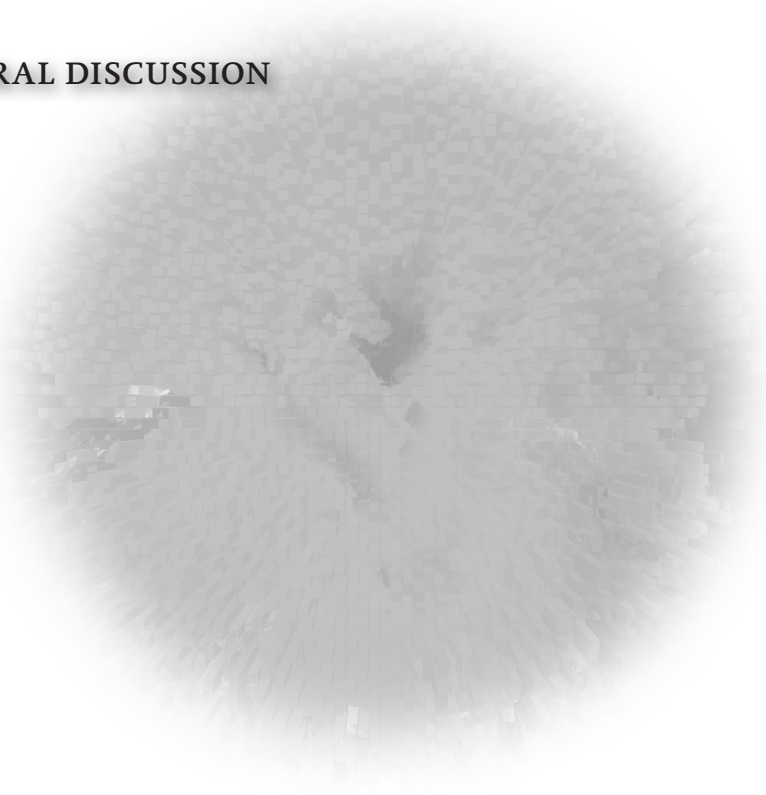
Chapter 7

General discussion



General discussion

Acute wound healing normally occurs in a predictable sequence of coagulation, inflammation, proliferation, remodelling, however, when the anatomic and functional integrity of the skin is not reached within 3 weeks, a wound is considered chronic or hard-to-heal.[1,2,3] Chronic wounds, including pressure ulcers, leg ulcers and diabetic foot ulcers are often painful and debilitating for patients, resulting in a reduction of quality of life.[4,5,6] Moreover, chronic wounds are associated with high costs accounting for more than 2-4% of health care expenses worldwide.[7] Within the next 40 years, the cost burden of treating chronic wounds is expected to grow progressively due to an aging population and in particular a sharp rise in the incidence of both obesity and diabetes.[8-11]

Prevalence of chronic wounds

Related to this burden of disease there is a need for more precise prevalence data about chronic wounds. Prevalence data can create awareness in caregivers, managers, policymakers and politicians. Subsequently, interventions to improve the care for patients with these wounds can be initiated. In the Netherlands and more specifically in Dutch nursing homes (NHs), the prevalence of (differentiated) chronic wounds has not been previously measured.[12] In this thesis, the prevalence of infected chronic wounds in Dutch nursing homes was assessed and, in addition, it was explored whether several institutional and ward related quality indicators of care related to these wounds, were fulfilled.

The results showed that in 21 participating nursing homes with 61 wards and 1514 patients, 63 patients had a total of 72 chronic wounds, resulting in an overall prevalence of 4.2%. Almost half (46%) of these wounds were pressure ulcers (PUs) followed by post-surgical wounds (9.5%). It also appeared that 22% (n=16) of these 72 chronic wounds were clinically assessed as infected. Although the 1514 residents represented 2.4% of the 63,000 nursing home residents living in Dutch nursing homes, the measured prevalence of chronic pressure ulcers (2.4%) was comparable with the prevalence figure described by Halfens et al. (2012) in an earlier study in a much larger population of care home residents in The Netherlands. Moreover, the characteristics (gender, age and BMI) of both Halfens' and our study population were comparable.[13]

Internationally, several attempts have been made[14-19] to assess the prevalence of (specific) chronic wounds. However, these earlier studies did not use uniform definitions and therefore comparisons of different prevalence figures are difficult and in fact impossible. Applying a uniform methodological approach like the Dutch National Prevalence Measurement of Care Problems (LPZ) is necessary to ensure a reliable data collection and to allow comparisons between health care settings; nationally and internationally.[20]

From our study it was also apparent that in the participating NHs a defined wound care policy had not been successfully implemented. Although at institutional level most structural quality indicators related to chronic wound care seemed to be fulfilled; at ward level this was not the case. The relevance of our study lies in the fact that, to our knowledge, this is the first one to measure structural quality indicators related to both the prevalence of as well as care of patients with chronic wounds in Dutch nursing homes.

Infection of chronic wounds

Infection is a relevant extrinsic factor in relation to the chronicity of wounds. In contrast to the overt signs and symptoms of acute wound infection, those of an infected chronic wound are more subtle and achieving precision in the clinical assessment of an infected chronic wound is challenging.

In order to provide structure to the identification of wound infection the use of criteria in addition to those accepted as 'traditional' have been proposed.[21] Validation of the suggested additional wound infection criteria has been undertaken in two separate studies.[22,23] Cutting illustrated the accuracy of the criteria reported by Cutting and Harding in 1994 whereby 39 out of 40 of the decisions made by the author on the infection status of the wounds were corroborated by wound semi-quantitative swab culture.[22] Although Gardner et al. arbitrarily modified and omitted some of the criteria, the study using quantitative microbiology was overall supportive of the secondary signs of infection as reported by Cutting and Harding in 1994.[23] Although many of the criteria did apply across the spectrum of most wound types, in 2005 the criteria were refined per wound type using a Delphi panel technique.[24]

In this thesis the top five clinical signs and/or symptoms of infection for different types of chronic wounds as ranked by Nursing Home Physicians (NHPs, nowadays called elderly care physicians) was compared with the rankings made by the international multidisciplinary Delphi group in 2005.[24] The results of our study showed first that NHPs mostly are involved in treating PUs and that they encounter other types of chronic wounds less frequently. Second, regarding the top five clinical signs and/or symptoms of wound infection as indicated by Dutch NHPs compared to the rankings of the international multidisciplinary Delphi group, the NHPs tended to hold more tight to 'traditional' clinical infection criteria such as 'pus/abscess' and 'malodour' when assessing chronic wound infection, while the Delphi group in this respect focused on 'cellulitis', 'delayed healing' and 'deterioration of the wound'/'wound breakdown'. The cause of this difference is not clear.

Nevertheless as mentioned, Dutch NHPs are generally more focussed on PUs than on any other type of chronic wound. Especially since in 2003 the Dutch Health Care Inspectorate declared the prevalence of PUs as a specific public and obligatory quality indicator of performance.[25] In the same year the Dutch Association of Elderly Care Physicians and Social Geriatricians launched a guideline, specifically for PUs (NVVA (now Verenso) 2003).[26] In this guideline, 'redness', 'swelling', 'warmth' and 'pus' as 'traditional' clinical infection criteria were indicated to assess infection of a PU. Therefore, it may be expected that NHPs will apply these criteria also to other types of chronic wounds.

Bacterial culture and quantification is a method to additionally assess the presence of a wound infection. A microbial growth greater than 10^5 CFU/g tissue or ml wound fluid has been considered indicative for wound infection.[27-31] Meanwhile, the number of microorganisms is held less important than the presence of bacteria employing quorum sensing to improve their virulence and persistence, and to finally overcome patient's immune response.[32,33] Quantitative analysis requires a reproducible and reliable method of wound sampling.

As part of this thesis a review of the literature was performed to assess the most valid and reliable swab technique for chronic wounds in comparison to a biopsy. Cooper has offered 'ten top-tips to support the caregiver taking a wound swab and designated the Levine technique as the preferential method.[34] Consecutively, the Levine swab technique was used in a prospective study executed in an outpatient wound clinic to explore whether swab results may support the clinical assessment of an infection of a chronic wound.[31,34] We concluded from the results of this study as described in chapter 4, that microbiological analysis of swabs from chronic wounds to support the clinical assessment of wound infection is a waste of time and money. The clinical assessments of 211 chronic wounds were not significantly correlated to the qualitative and semi-quantitative bacteriological results of the swabs taken. This applied for all types of chronic wounds, including patients with a known diagnosis of diabetes mellitus or peripheral arterial disease (PAD).

The discussion about the value of swab taking is however complicated by the fact that up to 90% of chronic wounds contains biofilm[35-37], which might not be successfully harvested by the swab or indeed culturable using standard culture techniques.[38-40] Although tissue biopsies in chronic wounds are considered to deliver more reliable microbiological samples because they also include bacteria present in a biofilm, taking biopsies is time-consuming in their analysis and invasive for patients.[40] Moreover, Serena et al. did not find a correlation between the clinical assessment and the results of quantitative microbiological cultures taken by a biopsy.[41] Although all 49 chronic venous leg ulcers (existence >1 month) in their study were clinically assessed as not infected, still 14 out of 49 (28%) biopsies scored a positive culture result. Other studies related to this issue are not available to the best of our knowledge. It is clear that reliable and feasible laboratory techniques are needed to support the clinical assessment of infected chronic wounds. However, it appears that the number of micro-organisms never leads to the diagnosis of wound infection per se. It is the products of bacteria, that is, the expression of 'virulence factors' which actually cause wound infection.[33]

Innovative wound care practice

Nowadays, worldwide a growing number of wound care centres are being established.[43-45] The emergence of these wound care centres reflects the size of the problem of chronic wounds as well as the increasing cost burden for health care systems. In addition to the delivering of high quality assessment and treatment at these wound care clinics, it is essential to establish a financially viable enterprise.[3,42-44] In 2009 the Knowledge Centre in Wound Care (KCWC) was founded in Venray, the Netherlands. Shortly after its introduction a cost-analysis study was conducted. The results showed that wound care for chronic wounds of patients was not only therapeutically effective (complete healing achieved in 106 out of 172 patients or 62%) but also cost-efficient. In a comparison between the year pre- and post-admission of patients, the base case analysis post-admission showed that considerable savings in reimbursement costs (€2,533 per patient, per year) were achieved. The results of this cost-analysis support the conclusion of studies conducted in Great Britain showing that treatment in leg ulcer clinics is more cost effective than treatment in hospital-based wound care clinics.[45-48] The Dutch Healthcare Authority has used the evaluation of the KCWC to advise the Ministry of Health, Welfare and Sport how to arrange and finance chronic wound care from 2015 onwards in the Netherlands.[47] Further prospective clinical and cost studies need to be performed to confirm the results of our study in the KCWC.[42,43,49,50]

Methodological considerations and limitations

Different methodologies were used in this thesis. In **chapter 2**, a cross-sectional descriptive survey was conducted, using the information from self-reported questionnaires in a sample of all Dutch NHPs (361), taken from the list of the Dutch Association of Nursing Home physicians (now Verenso at Utrecht, the Netherlands). The questionnaire was designed to collect both quantitative and qualitative information. NHPs were asked to indicate the number of specific chronic wounds they were treating and to choose their five most important clinical symptoms of chronic wound infection per wound type out of a list of criteria.[24] This methodology might be biased by the subjectivity of the answers given by the NHPs, the ambiguity of the definitions used and the term 'importance' in relation to the ranking of signs and symptoms of chronic wound infection. Despite this, the methodology was acceptable for our aim to do primarily a first explorative study.[51,52]

In **chapter 3** the prevalence of (infected) chronic wounds was measured in a cross sectional way using the methodology of the National Prevalence Measurement of care problems of Maastricht University (LPZ-Landelijke Prevalentiemeting Zorgproblemen).[53] To assess the integral impact of a relevant care problem on patient, care organisational and societal level, prevalence measurements of this care problem, e.g. the problem of chronic wounds, are useful. By applying a methodological approach like the LPZ measurement, it is ensured that the data obtained can be used for benchmarking within and between health care settings. The cross-sectional design of this measurement however, does not allow us to draw causal conclusions. Nevertheless this approach is a good basis for more in depth quantitative and qualitative research.[20]

In the literature review on the validity and reliability of a wound swab in comparison to a biopsy taken from chronic wounds described in **chapter 4**, it was anticipated that a systematic search would not provide many hits. Therefore the scope of search for peer reviewed articles was widened to include articles on non-infected and acute wounds. Of the eight articles found, only six contributed to the conclusion of the article, clearly indicating that there is a low evidence base on this issue.

In the open non-randomised experimental study described in **chapter 5** it appeared that local antiseptics were frequently used as part of the patient's wound treatment plan. This might have had a negative effect on the study results. Therefore 68 (32%) of all wounds, not treated with antimicrobials in the period of two weeks before the clinical assessment, were analyzed separately. This analysis showed that 34 (50.0%) of these 68 wounds were clinically assessed as infected, whereas 58 had a positive qualitative swab result. As for the entire sample of 211 chronic wounds, also for these 68 wounds no significant relationship was found between the clinical assessments and the results of the swabs assessments (Chi-square; p-value >0.05). It appeared, therefore, that the use of local antiseptics and systemic antibiotics did not influence our final results.

The cost analysis in **chapter 6** involved only one outpatient wound clinic, in one region in the Netherlands. Because the distribution of cost data was skewed, non-parametric bootstrapping was used to test for statistical differences in costs between the periods of one year before and one year after admission to the wound clinic.[54]

The cost-analysis was limited by the exclusive use of the database of one insurance company Coöperatie Volksgezondheidszorg (VGZ) and the inability to include reimbursement costs related to data falling under the Exceptional Medical Expenses Act (AWBZ). To determine the likely impact of using an alternative value of variables, four sensitivity analyses and a subgroup analysis were performed. A prospective study design, using incident registration for the recording of patient data, wounds and costs, is necessary to be able to draw more firm conclusions regarding the effects of an outpatient wound clinic on noticeable changes in reimbursement costs.

Implications for daily wound care practice

Following our prevalence study and the studies related to the assessment of infected chronic wounds, the following recommendations can be given for clinical practice.The prevalence figure of 4.2% for chronic wounds was the first prevalence figure of chronic wounds in the Dutch nursing home sector. A regular prevalence measurement of chronic wounds may create more awareness and focus among managers and caregivers. This may support the actual daily wound care activities, a better registration of these wounds in the resident's files, the multidisciplinary discussions on chronic wounds as well as other improvement activities in the care for residents with chronic wounds. Regular audits of the quality of wound care may ultimately lead to a higher level of basic care performance.[20]

From the studies in this thesis it may be concluded that swab assessments are not supportive for the clinical assessment of infected chronic wounds. Lacking a real 'Gold' standard, the assessment of chronic wound infection still relies heavily on the clinical assessment. Although the World Union of Wound Healing Societies (WUWHS) consensus document provides broad and safe guidance on the areas of diagnosis and topical/systemic treatment of bacterial wound infection, it remains a consensus opinion of an international panel of experts. Therefore the signs and symptoms of this panel need further validation.[55,56]

Implications for future research

To create more awareness of and focus on chronic wounds, regular and uniform audits such as the National Prevalence Measurement of Care Problems (LPZ) should be performed in all health care settings because these are the basis for targeted care improvement programs. Moreover these audits may support burden of disease studies, related to these care problems. Regarding the issue of diagnosing infection of chronic wounds and knowing that there is currently no better diagnostic strategy than the clinical assessment itself, there is a need of more research into innovative objective diagnostic solutions. One of the most promising advances is the use of DNA sequencing techniques. Potential pathogens could be detected by molecular microbial diagnostic approaches such as polymerase chain reaction (PCR) and 16S ribosomal probes.[57-60,61] A retrospective study revealed that antimicrobial therapy guided by molecular diagnosis, in comparison with the use of swabs, may have a statistically and clinically significant shorter healing time (45.9%).[58] However, at this moment, the high costs and the complicated feasibility of these techniques to use in for instance nursing home settings, do not allow extensive use yet.

Conducting further prospective designed studies is necessary to demonstrate the possible benefit of DNA sequencing in assessing infection of chronic wounds. Biofilms are present in most chronic wounds, in which they subsequently maintain an inflammatory response.[35] The issue of addressing whether or not chronic wounds are 'infected' is controversial. This controversy specifically relies on the traditional diagnostic markers of infection of Celsus (rubor, tumor, calor and dolor). Maybe the term 'infection' requires redefining in light of insight in the prevalence and behaviour of a biofilm. Specific techniques as scanning electron microscopy or confocal laser scanning microscopy are necessary to visualize the presence of bacteria in a biofilm, because they cannot be seen by naked eye or microscope.[35,40]

However common secondary signs of infection as excessive exudate, slough, tunnelling and undermining, maceration of the wound edge along with pain, swelling and deterioration may suggest an active biofilm.[62] To include the potential presence of biofilms for use in informing clinical practice decisions, biofilm characteristics supporting those decisions need standardized definitions and valid evidence that they predict or diagnose healing or infection outcomes. Future research is needed to provide a rapid accurate technique to identify and characterize biofilms in a way that optimizes their validity in assessing and screening patients' risk of infection or delayed healing and to support clinical decisions.

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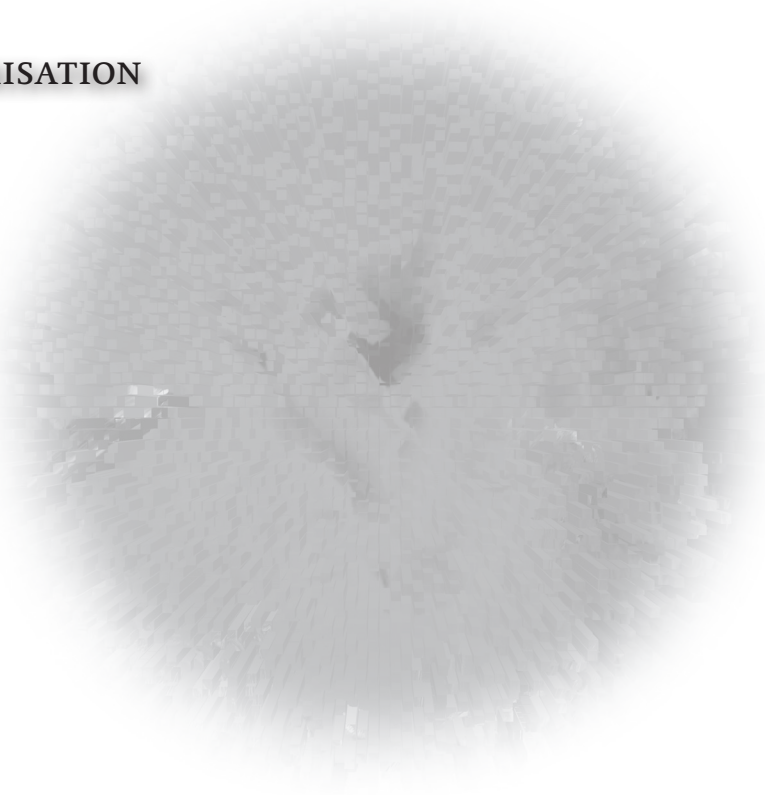
Chapter 8

Valorisation



Valorisation

Societal relevance

Chronic wounds, like pressure ulcers, leg ulcers and diabetic foot ulcers are often painful and debilitating for patients, resulting in a reduction of quality of life. Moreover, chronic wounds are associated with high costs accounting for more than 2-4% of health care expenses worldwide. Within the next 40 years, the cost burden of treating chronic wounds is expected to grow progressively due to an aging population and in particular a rise in the incidence of both obesity and diabetes. To assess the integral impact of this relevant care problem on patient, organisational care and societal level, prevalence and quality care measurements are useful to create awareness in caregivers, managers, policymakers and politicians of the scale of the problem **chapter 2**.

By applying a methodological approach like the National Prevalence Measurement of Care problems of Maastricht University (LPZ-Landelijke Prevalentiemeting Zorgproblemen) on the problem of (infected) chronic wounds, it is ensured that the data obtained can be used for benchmarking within and between health care settings. Before publication of this thesis, to the best of our knowledge no prevalence data and data about the quality of care related to patients with (infected) chronic wounds were available in the Netherlands **chapter 3**.

Chronic wounds may be complicated by infection, ultimately resulting in tissue damage and delayed healing. Efficient management and careful antimicrobial treatment of these infected wounds is essential and associated with earlier wound healing and less costs. However, the clinical assessment of a chronic wound infection is challenging. The clinical signs and symptoms of infection of chronic wounds are difficult to interpret. Therefore the clinical assessment is often accompanied by the identification and assessment of the number of microorganisms isolated from the wound.

In this thesis the literature was reviewed to explore the usefulness of a wound swab (using the Levine or Z-technique) in comparison to a biopsy as a reliable method for the diagnosis of a chronic wound infection. Compared both with the biopsy as golden standard, the diagnostic accuracy to diagnose a chronic wound infection by the Levine's technique showed to be higher in comparison to the Z-technique **chapter 4**.

The Levine swab technique was used in an additional study to assess whether bacteriological analysis of a wound swab is supportive in the clinical assessment of infection of a chronic wound. The results of that study showed that the clinical assessments were not significantly correlated with the bacteriological results of the swabs taken. The conclusion was that in our study microbiological analysis of swabs taken from chronic wounds does not support the clinical assessment, and in fact seems to be a waste of time and money **chapter 5**.

The results of a cost analysis of one of the first outpatient community wound care clinics in the Netherlands, the Knowledge Centre in Wound Care (KCWC) in Venray have been described in **chapter 6**. The differences in costs related to wound care between the year before and the year after initial admission to the wound clinic resulted in a reduction of €2,553 per patient, per year in the base case analysis.

This study was a first attempt of a cost analysis of an equipped outpatient wound clinic in the Netherlands. The organization of more outpatient wound clinics in the Netherlands may be an adequate and cost effective solution to meet the forthcoming growth of chronic wounds.

Usability of the results for daily practice

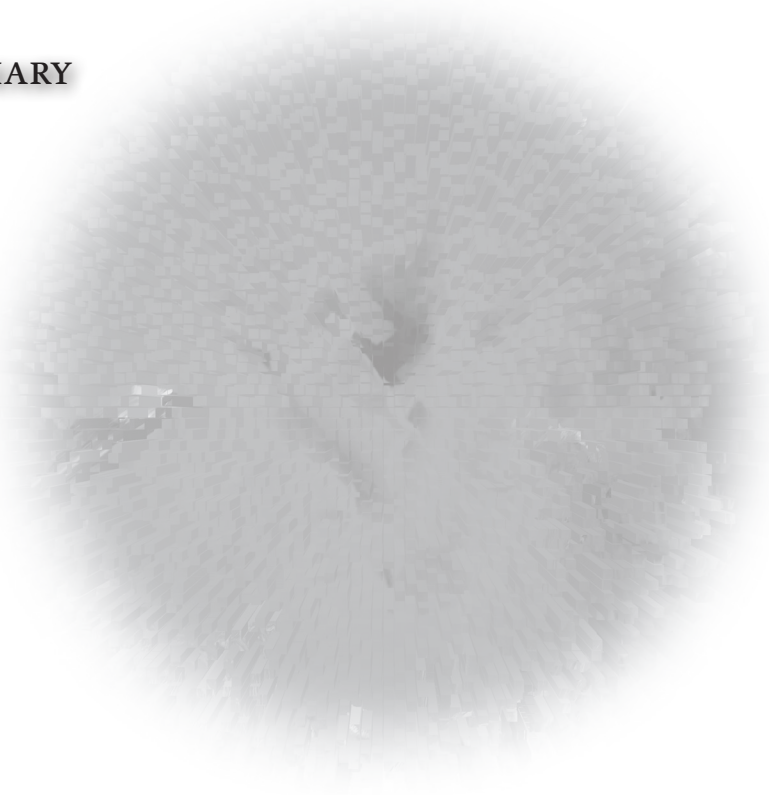
Regular prevalence and quality of care measurements related to the problem of chronic wounds will create more awareness and focus among managers and caregivers. This will support actual daily wound care activities, e.g. the multidisciplinary discussions on chronic wounds as well as other improvement activities in the care for residents with chronic wounds. Applying a uniform methodological approach like the Dutch National Prevalence Measurement of Care Problems is necessary to ensure a reliable data collection and to allow comparisons between health care settings; nationally and even internationally **chapter 3.**

One of the conclusions of this thesis was that microbiological analysis of swabs taken from chronic wounds does not support the clinical assessment, and in fact seems to be a waste of time and money **chapter 5**. Naturally, conducting further research is necessary to affirm the results of this thesis, and to be able to generalise its conclusion. Knowing there is currently no better diagnostic strategy than the clinical assessment, and that the interpretation of signs and symptoms of infection of a chronic wound is not easy, elderly care physicians and other wound care related professionals need further education. Differentiated education programs, in terms of knowledge and skills in clinically assessing infected chronic wounds must be developed, both for registered physicians as students.

Knowing that there is currently no better diagnostic strategy than the clinical assessment itself, there is also need of research into innovative diagnostic solutions. A promising development is the use of DNA sequencing techniques. However related high costs and the complicated feasibility of these techniques to use in for instance nursing home settings, do not allow extensive use yet **chapter 5**.

The emergence of a worldwide growing number of wound care centres reflects the relevance of the problem of chronic wounds as well as the increasing cost burden for health care systems. The results of the cost-analysis of one outpatient wound clinic in this thesis showed that wound care was not only therapeutically effective (complete healing in 106 out of 172 patients) but also cost-efficient. In a comparison between the year pre- and post-admission of patients, the base case analysis post-admission showed that considerable savings in reimbursement costs (€2,533 per patient, per year) were achieved. In accordance with the recommendations of van Mierlo-van de Broek (2011): a timely referral of a patient with a chronic wound to a genuine wound care specialist team/wound care centre in which a comprehensive multidisciplinary wound assessment is performed, followed by a strictly monitored and targeted intervention, seems to have benefits for both the patient and the society **chapter 6**.

Summary



Summary

The studies in this thesis were set up to investigate the prevalence of (infected) chronic wounds in Dutch nursing homes, and to answer the question whether a swab is a valid and reliable method for the assessment of infection of a chronic wound. At the end the results of a cost analysis of the Knowledge Centre of Wound Care in Venray are provided.

Wound healing normally occurs in a predictable sequence (coagulation, inflammation, proliferation, remodelling). When the anatomic and functional integrity of the skin is not reached within 3 weeks, a wound is considered chronic or hard-to-heal.

Chronic wounds, including pressure ulcers, leg ulcers and diabetic foot ulcers are often painful and debilitating for patients, resulting in a reduction of quality of life. Moreover, chronic wounds are associated with high costs accounting for more than 2-4% of health care expenses worldwide. Within the next 40 years, the cost burden of treating chronic wounds is expected to grow progressively due to an aging population and in particular a sharp rise in the incidence of both obesity and diabetes.

To create awareness in caregivers, managers, policymakers and politicians of the scale of the problem, there is a need for prevalence data of chronic (infected) wounds. Up until now, no data have been published in the Netherlands.

Chronic wounds may become complicated by infection.Wound infection leads to a multiplication of micro-organisms, a prolonged (and excessive) inflammatory response, a delay in the collagen synthesis, and a retarded epithelialisation. It ultimately results in tissue damage. Efficient management and careful antimicrobial treatment of these wounds is essential. This leads to earlier wound healing and costs less. However, the clinical assessment of a chronic wound infection is challenging. In comparison with the clinical assessment of infection of acute wounds, the clinical signs and symptoms of infection of chronic wounds are more difficult to interpret.

The clinical assessment of chronic infected wounds is often accompanied by the identification and the assessment of the number of present isolated microorganisms. It has been claimed that bacterial quantification supports the clinical assessment of wound infection supports and is useful for a focused treatment of the wound.

Following her 'Exploration of Dutch wound care', van Mierlo-van den Broek (2011) recommended an innovative organization of chronic wound care in the Netherlands. The key elements of this innovative way of organizing wound care involved the possibility of a quick referral of a patient with a chronic wound to a genuine wound care specialist team/ wound care centre in which a comprehensive multidisciplinary wound assessment is performed, followed by a strictly monitored and targeted intervention targeted and strictly monitored wound treatment plan. In succession of several cost effective examples of community based leg ulcer clinics in the UK at the end of last century an outpatient wound clinic, the Knowledge Centre in Wound Care (KCWC) was founded in Venray, the Netherlands in 2009. Although the phenomenon of an outpatient wound clinic meets the substantive argument for an innovative organization of chronic wound care in the Netherlands, it is not clear whether such an approach is cost-effective.

Chapter 1 the general introduction addresses background information on the knowledge of chronic wounds and wound infection In addition the aims and outline of the thesis are presented.

In **chapter 2** using a cross-sectional descriptive survey, a first explorative study was conducted to investigate the number and types of chronic wounds treated by Dutch Elderly care physicians (former Nursing Home Physicians or NHPs). The study was also aimed to identify how many of the treated chronic wounds the NHPs considered infected. 361 NHPs were sent a questionnaire to select and rank their top five criteria for chronic wound infection from a list that was provided. The signs and symptoms on the provided list were the same as those indicated by the European Wound Management Association's position document in 2005. 139 of the NHPs returned the questionnaire and 121 were valid to use in the analysis. Then their ranking was compared with the selections made by an international multidisciplinary Delphi group of wound experts in 2005. It showed that at the time of the survey, 73.5% of the responding NHPs treated at least one chronic pressure ulcer (PU). 31.6% of the NHPs treated at least one, but no more than two chronic post-operative wounds. Chronic venous leg ulcers (VLUs), arterial ulcers and diabetic ulcers were being treated less frequently than PUs and post-operative wounds. Of the PUs, 53% were considered to be infected. The other chronic wounds were considered to be infected far less frequently. In comparison to the group of international wound experts, Dutch NHPs appeared to use more 'traditional' criteria such as 'puss/abscess' and 'malodour' to identify chronic wound infection.

In **chapter 3** the prevalence of (infected) chronic wounds was described more extensively. It was also explored which signs and symptoms were used to diagnose infected chronic wounds. In April 2012, as part of the annual National Prevalence Measurement of Care Problems of Maastricht University (LPZ), a multi-centre cross-sectional point-prevalence measurement was carried out together with an assessment of relevant care quality indicators. The results showed that in 21 participating nursing homes with 61 wards and 1514 patients, 63 patients had together 72 chronic wounds, resulting in an overall prevalence of 4.2%. Almost half (46%) of these wounds were pressure ulcers (PUs) followed by post-surgical wounds (9.5%). 22% (n=16) of these 72 chronic wounds were clinically assessed to be infected. Increase of exudate (81.3%; n=13), erythema (68.8% ; n=11), pain (56.3%; n=9) and wound recalcitrance (56.3%; n=9) were considered to be diagnostic signs and symptoms of infection. It showed that at institutional level most quality indicators were fulfilled. In all the nursing homes the number of chronic wounds were centrally registered and every two years a specific training was organized. However, at ward level the same quality indicators were fulfilled less.

It was the aim in **chapter 4** by reviewing the literature to investigate the usefulness of a wound swab (using the Levine or Z-technique) in comparison to a biopsy as a reliable method for the diagnosis of a chronic wound infection.

The electronic databases PubMed, the Cumulative Index of Nursing and Allied Health Literature (CINAHL) and Medline were searched by strategy. Only 6 articles fulfilled the inclusion criteria. The Levine technique detects more organisms in acute wounds as well as in chronic wounds. At a threshold of $3.7x10^4$ micro-organisms per swab, the Levine technique had a sensitivity of 0.90 an a specificity of 57%, and a positive predictive value and negative predictive value of 0.77 and 0.91 respectively. Compared both with the biopsy as golden standard, the diagnostic accuracy to diagnose a chronic wound infection by the Levine's technique was higher in comparison to the Z-technique. From the international literature it became clear that the method of swab taking varied and was not uniformly described.

In **chapter 5** in a prospective study the Levine swab technique was used to assess whether bacteriological analysis of a wound swab is supportive in the clinical assessment of infection of a chronic wound. Patients attending an outpatient wound clinic who had endured a chronic wound for more than three weeks were clinically assessed for infection. The13 signs and symptoms of chronic wound infection, mentioned in the international consensus document on wound infection of the World Union of Wound Healing Societies (WUWHS) were used (2008). Standardized wound swabs were taken by the Levine technique. The microbiological findings of the swabs were compared with the clinical assessment of the wounds.The results showed that the clinical assessments were not significantly correlated with the bacteriological results of the swabs taken. This applied for all types of chronic wounds, including for those of patients with a known diagnosis of diabetes mellitus or peripheral arterial disease (PAD). The conclusion was that in our study microbiological analysis of swabs taken from chronic wounds do not support the clinical assessment, and in fact is waste of time and money.

Chapter 6 described the results of a cost analysis of one of the first outpatient community wound care clinics in the Netherlands, the Knowledge Centre in Wound Care (KCWC) at Venray. An observational cohort study was conducted with a one-year pre-admission and a one-year post-admission comparison of costs. Patients were included after their initial admission at the outpatient wound care clinic. Only patients insured by the health insurance company Coöperatie Volksgezondheidszorg (VGZ) were included. A standard six-step procedure for performing cost studies was used to calculate the costs. Given the skewed data, non-parametric bootstrapping was used to test for statistical differences. The results showed that wound care at the KCWC for chronic wounds of patients was not only therapeutically effective (complete healing in 106 out of 172 patients) but also cost-efficient. The differences in costs related to wound care between the year before and the year after initial admission to the wound clinic resulted in a reduction of €2,533 per patient, per year in the base case analysis. This study was a first attempt of a cost analysis of an equipped outpatient wound clinic in the Netherlands. The organization of more outpatient wound clinics may be an adequate solution to meet the expected growth of chronic wounds in the Netherlands.

Chapter 7 provides an overview and discussion of the main results presented in of this thesis. Theoretical and methodological considerations were addressed. The implications for daily wound care practice and future research are described. Furthermore, the following recommendations are made:

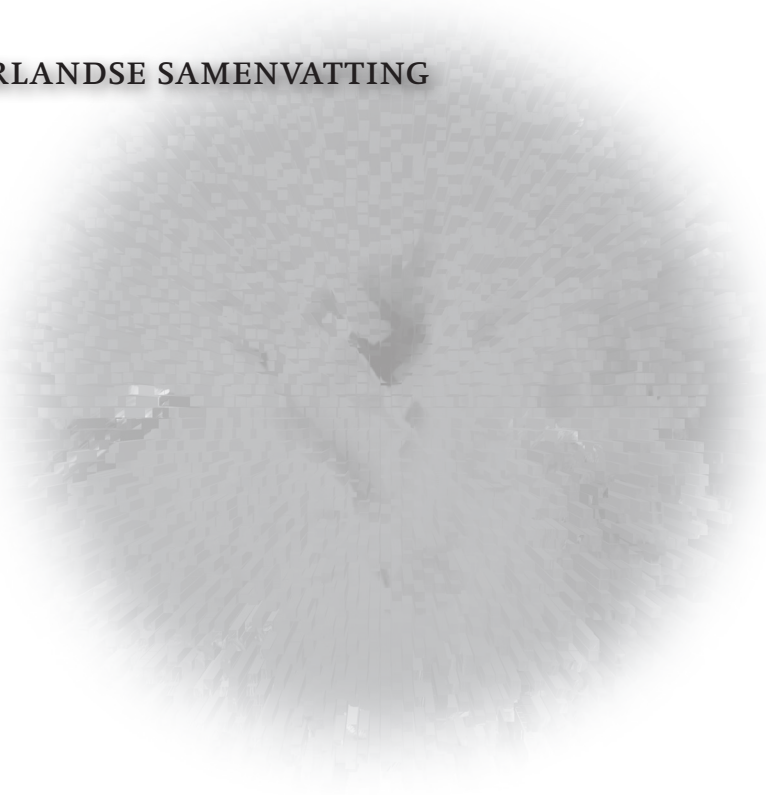
1) Conduct a regular prevalence measurement of chronic wounds. This may create more awareness and focus among managers and caregivers and will support the actual daily wound care activities, a better registration of these wounds in the resident's files, the multidisciplinary discussions as well as other improvement activities in the care for residents with chronic wounds.

By applying a methodology approach like the National Prevalence Measurement of care problems of Maastricht University (LPZ-Landelijke Prevalentiemeting Zorgproblemen) it is ensured that the data obtained can be used for benchmarking within and between health care settings.

2) Validate the signs and symptoms further that are provided by the consensus document 'Wound infection in clinical practice' of the World Union of Wound Healing Societies (WUWHS) in 2008.

Regarding the issue of diagnosing infection of chronic wounds and knowing that there is currently no better diagnostic strategy than the clinical assessment itself, there is need of research into innovative objective diagnostic solutions. A promising advance is the use of DNA sequencing techniques. However related high costs and the complicated feasibility of these techniques to use in for instance nursing home settings, do not allow extensive use yet.

Nederlandse samenvatting



Nederlandse samenvatting

Prevalentie en beoordeling van (geïnfecteerde) chronische wonden

De studies in dit proefschrift zijn opgezet om achtereenvolgens de prevalentie van (geïnfecteerde) chronische wonden in Nederlandse verpleeghuizen te onderzoeken en om de vraag te beantwoorden of een wond swab een valide en betrouwbare methode is ter beoordeling van een infectie van een chronische wond. Tot slot is een kostenanalyse gemaakt van de kosten van behandeling in het Kenniscentrum Wondbehandeling in Venray. Normaliter treedt wondgenezing op in een voorspelbare volgorde (reactie-, regeneratie-, en rijpingsfase). Wanneer de genezing van een wond op zich laat wachten en de anatomische en functionele integriteit van de huid niet binnen 3 weken bereikt is, wordt de wond als chronisch of 'hard-to-heal' beschouwd.

Chronische wonden, zoals doorligwonden (decubitus), een open been (beenzweer, ulcus cruris) en een diabetische voet, zijn vaak pijnlijk en leveren beperkingen en handicaps op waardoor een patiënt vaak een vermindering van zijn levenskwaliteit ervaart. Chronische wonden zijn ook geassocieerd met hoge kosten. Wereldwijd worden de kosten geschat op 2-4% van het gezondheidszorgbudget. In de komende 40 jaar, zullen de kosten van behandeling van chronische wonden naar verwachting nog verder stijgen. Oorzaak hiervan is de toename van het aandeel 80-plussers binnen de groep mensen van 65 jaar en ouder ('de dubbele vergrijzing') en een stijging van de incidentie van obesitas en diabetes mellitus.

Om onder andere zorgverleners, managers, beleidsmakers en ook politici bewust te maken van de omvang van het probleem van (geïnfecteerde) chronische wonden zijn gegevens zoals prevalentiecijfers hierover nodig. Tot nog toe zijn deze gegevens over (geïnfecteerde) chronische wonden in Nederland maar beperkt beschikbaar.

Chronische wonden kunnen geïnfecteerd raken waarbij de wondinfectie leidt tot een vermeerdering van micro-organismen, die op hun beurt zorgen voor een langdurige en heftige ontstekingsreactie, een vertraagde collageensynthese en een vertraagde epithelialisatie. Wondinfectie leidt tot weefselschade.

Een effectieve en efficiënte antimicrobiële behandeling bij een geïnfecteerde wond is daarom essentieel. Door een dergelijke behandeling genezen wonden niet alleen sneller, maar leveren zij ook minder zorgkosten op en minder productieverlies door ziekteverzuim. De klinische beoordeling van een infectie van een chronische wond is echter moeilijk. De symptomen van een geïnfecteerde chronische wond zijn minder gemakkelijk te interpreteren dan de infectiesymptomen van een acute wond.

In aanvulling op een klinische evaluatie van een geïnfecteerde wond wordt daarom vaak een microbiële analyse van het aantal en soort aanwezige micro-organismen verricht. Met behulp van deze kwantificatie en kwalificatie van bacteriën zou men beter in staat zijn om een wondinfectie vast te stellen en de wond 'op maat' te behandelen.

Van Mierlo-van den Broek gaf naar aanleiding van haar 'Verkenning van de wondbehandeling in Nederland', in 2011 het advies om in Nederland de behandeling van chronische wonden anders te organiseren.

De belangrijkste elementen van haar voorstel zijn: het creëren van een snelle verwijzing van een patiënt met een chronische wond naar een team van specialisten / wond expertise centrum; de optie voor een multidisciplinaire beoordeling, gevolgd door een specifieke en goed geregisseerde behandeling. In navolging van een aantal goede voorbeelden in het Verenigd Koninkrijk in de jaren '90, werd in Nederland in Venray (2009), het Kenniscentrum Wondbehandeling (KWB) opgericht. Het KWB lijkt inhoudelijk te voldoen aan het advies van van Mierlo-van den Broek. Het was echter niet duidelijk of de behandeling en zorg die vanuit het KWB geleverd wordt, kosteneffectief is.

Hoofdstuk 1 geeft een algemene inleiding en achtergrondinformatie van de begrippen 'chronische wond' en 'wondinfectie'. Daarnaast worden de verschillende doelstellingen en de opzet van het proefschrift besproken.

In **hoofdstuk 2** is een cross-sectioneel beschrijvend onderzoek beschreven om de soort en het voorkomen van chronische wonden in Nederlandse verpleeghuizen te onderzoeken. De studie had ook tot doel om een indruk te krijgen over het aantal wonden dat door specialisten ouderengeneeskunde (voorheen verpleeghuisartsen genoemd) als geïnfecteerd geduid wordt. 361 specialisten ouderengeneeskunde (SOs) werden gevraagd de door hen gebruikte infectiesymptomen te selecteren en te rangschikken in een top vijf. Selectie gebeurde op basis van een aan hen van tevoren verstrekte lijst met symptomen. 139 artsen retourneerden de vragenlijst waarvan er 121 bruikbaar waren voor analyse. De resultaten werden vervolgens vergeleken met de selectie en rangorde gemaakt door een Delphi-panel bestaande uit een multidisciplinaire groep van internationale erkende experts in 2005.

Uit de enquête bleek dat 73,5% van de SOs, tenminste één chronische decubitus wond (PU) behandelde op dat moment. 31,6% van de SOs behandelde ten minste één, maar niet meer dan twee chronische postoperatieve wonden. Chronische open benen en een diabetische voet werden door SOs minder vaak behandeld dan doorligwonden en postoperatieve wonden. Van de doorligwonden, werden er 53% geduid als geïnfecteerd. De andere chronische wonden werden minder vaak als geïnfecteerd beschouwd. Het bleek dat de SOs meer dan de internationale experts gebruik maken van 'traditionele' criteria zoals 'pus / abces' en 'onwelriekende geur' om een aanwezige infectie van een chronische wond te duiden.

In **hoofdstuk 3** is de prevalentie van chronisch (geïnfecteerde) wonden uitgebreider beschreven, evenals de symptomen die gebruikt werden om een mogelijk infectie van een chronische wond te beoordelen. In april 2012, werd als onderdeel van de jaarlijkse Landelijke Prevalentiemeting Zorgproblemen van de Universiteit Maastricht (LPZ) een multicenter, cross-sectionele, punt-prevalentie meting uitgevoerd. Tevens werden een aantal kwaliteitsindicatoren gemeten. De resultaten toonden aan dat in 21 deelnemende verpleeghuizen met 61 afdelingen en 1.514 patiënten, 63 patiënten in totaal 72 chronische wonden hadden. Dit betekent een prevalentie van 4,2%.

Bijna de helft (46%) van deze wonden betrof doorligwonden, gevolgd door postoperatieve wonden (9,5%). 22% (n = 16) van deze 72 chronische wonden werd klinisch als geïnfecteerd beoordeeld.

Toename van wondvocht/pus (81,3%; n = 13), 'roodheid' (68,8%; n = 11), 'pijn' (56,3%; n = 9) en 'vertraagde genezing' (56,3%; n = 9) werden als diagnostische symptomen van een geïnfecteerde chronische wond genoemd. Op het niveau van de zorginstelling werd aan de meeste kwaliteitsindicatoren voldaan. In alle instellingen was een verantwoordelijke die het protocol /de richtlijn chronische wond up-to-date houdt, werden chronische wonden centraal geregistreerd en werd minstens elke twee jaar een bijscholing of themabijeenkomst georganiseerd. Op afdelingsniveau werd echter minder vaak voldaan aan deze kwaliteitsindicatoren.

De doelstelling van de literatuurstudie in **hoofdstuk 4** was om na te gaan of een wond swab (de Levine of Z-techniek), in vergelijking met een biopsie, een betrouwbare methode is, om vast te stellen of een chronische wond geïnfecteerd is. De elektronische databanken PubMed, de Cumulatieve Index of Nursing en Allied Health Literature (CINAHL) en Medline werden hiervoor systematisch doorzocht. 6 artikelen voldeden aan de inclusiecriteria. De diagnostische betrouwbaarheid van een wond swab afgenomen met de Levine techniek bleek, in vergelijking met de biopsie als 'Gouden standaard', hoger dan bij afname met de Z-techniek. De Levine techniek detecteert meer organismen in zowel acute wonden als chronische wonden dan de Z-techniek. Bij een drempel van $3.7x10^4$ micro-organismen per wond swab had de Levine techniek een sensitiviteit van 90%, een specificiteit van 57% en een positieve voorspellende waarde en negatieve voorspellende waarde van respectievelijk 0,77 en 0,91. Uit de internationale literatuur bleek ook dat de beschrijving van de methode van afname van een wond swab sterk varieert.

Vervolgens werd in **hoofdstuk 5** in een prospectieve studie de Levine techniek gebruikt om te onderzoeken of een microbiologische wond analyse de klinische beoordeling van het wel of niet geïnfecteerd zijn van een chronische wond kan ondersteunen. Bij deze beoordeling werd gebruik gemaakt van de 13 symptomen die beschreven zijn in het internationale consensus document van de World Union of Wound Healing Societies (WUWHS) in 2008. Gestandaardiseerd werden wond swabs afgenomen met de Levine techniek.

De microbiologische resultaten van de wond swabs werden vergeleken met de klinische beoordeling. Uit de resultaten bleek dat de bacteriologische uitkomsten van de afgenomen wond swabs niet met de klinisch beoordeling overeen kwam. Dit gold ook voor de chronische wonden van diabetici of van patiënten met perifeer arterieel vaatlijden (PAD). De conclusie van deze studie was dan ook dat afname en microbiologische analyse van wond swabs bij chronische wonden een verspilling van tijd en geld is. Wond swabs blijken in deze studie de klinische beoordeling van het wel of niet geïnfecteerd zijn van een chronische wond niet te ondersteunen.

In **hoofdstuk 6** is een kostenanalyse van de behandelingen in het Kenniscentrum Wondbehandeling (KWB) in Venray uitgevoerd, vanuit het perspectief van de zorgverzekeraar. Hiervoor werd een observationele cohort studie uitgevoerd. De zorgkosten van cliënten één jaar voorafgaand aan het eerste consult in het KWB werden vergeleken met de kosten gemaakt in het jaar daarna. Patiënten werden geïncludeerd na hun 1e consult mits zij verzekerd waren bij zorgverzekeraar Coöperatie Volksgezondheidszorg (VGZ). Om de kosten te berekenen werd gebruik gemaakt van een gestandaardiseerde zes-stappen procedure. De niet-Gaussiaanse verdeling van de kosten, was aanleiding om niet-parametrische bootstrapping te gebruiken om op aanwezige statistische verschillen te toetsen. De resultaten toonden aan dat wondbehandeling voor chronische wonden in het KWB, niet alleen therapeutisch effectief was (106 van de 172 patiënten genazen volledig) maar ook kosteneffectief. Het verschil in kosten tussen de zorgverlening het jaar voorafgaand en het jaar daarna liet in de base case analyse een vermindering van € 2.533 per patiënt per jaar zien. De kostenanalyse in deze studie was de eerste die verricht is in een 1e lijns wondkliniek. Op basis van de resultaten lijkt een 1e lijns wondkliniek zoals deze is georganiseerd in Venray een manier om zowel therapeutisch als financieel aan de verwachte toename in aantal chronische wonden tegemoet te kunnen komen.

Hoofdstuk 7 geeft een overzicht en bespreking van de belangrijkste resultaten die in de eerdere hoofdstukken van dit proefschrift aan bod zijn gekomen. Theoretische en methodologische beschouwingen worden gegeven. De gevolgen voor de dagelijkse praktijk en toekomstig onderzoek worden beschreven.

Bovendien worden de volgende aanbevelingen gedaan:

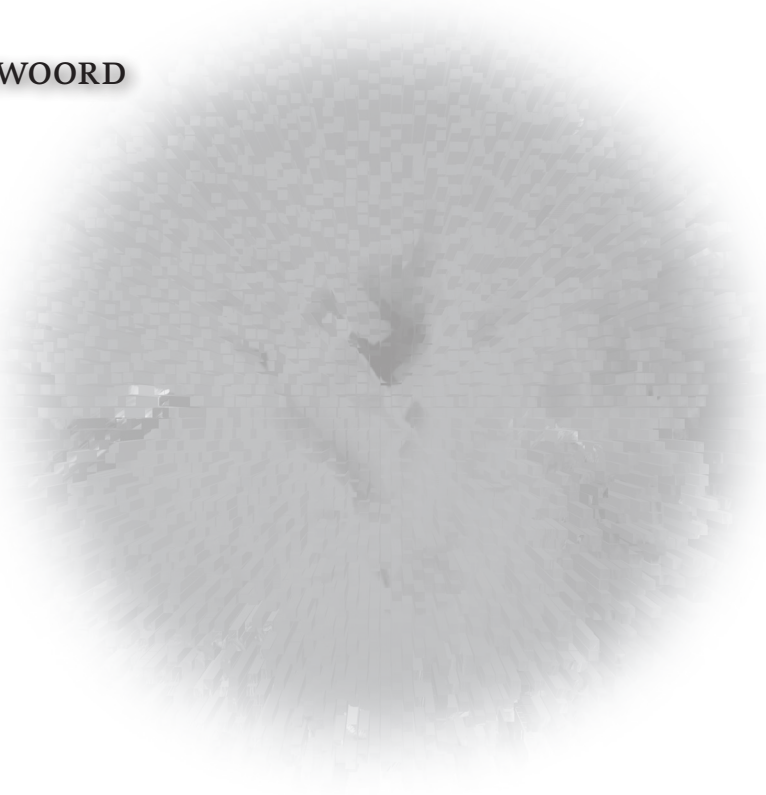
1) Meet regelmatig de prevalentie van chronische wonden. Dit kan leiden tot meer bewustwording en focus bij managers en verzorgers én zal de dagelijkse zorgactiviteiten voor cliënten met chronische wonden ondersteunen: een betere registratie in de dossiers van de patiënten, multidisciplinaire besprekingen, evenals andere verbeteringen in de zorg voor patiënten met chronische wonden.

Door toepassing van de Landelijke Prevalentiemeting Zorgproblemen van de Universiteit Maastricht, kunnen de meetresultaten ter vergelijking binnen eigen zorginstelling, maar ook tussen verschillende zorginstellingen, gebruikt worden.

2) Valideer de symptomen omschreven door de World Union of Wound Healing Societies (2008). Momenteel lijkt het klinische oordeel de best mogelijke diagnostische optie om een infectie van een chronische wond vast te stellen.

Er is daarnaast wel behoefte aan meer innovatief onderzoek naar objectieve diagnostische mogelijkheden, zoals de DNA-sequencing techniek. Deze is echter door zijn complexiteit en hoge kosten (nog) géén optie voor grootschalig gebruik in bijvoorbeeld verpleeghuizen.

Dankwoord



Dankwoord

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About the author

About the author

Armand Rondas was born in Maastricht on November 22th 1961. After graduating from secondary school in 1980 at the Jeanne d' Arc Lyceum at Maastricht he started his medical education in Belgium at the Hasselt University. After three years he graduated as candidate (Kandidaatsexamen).

In 1985 he moved to Amsterdam, to study Medical Biology, in which he graduated in 1987. In 1987 he attended the Medical School at the University of Amsterdam to continue his medical education and to graduate for his MD in 1988. In 1991 he started the post graduate medical specialization to become elderly care physician, at the Free University of Amsterdam (Vrije Universiteit Amsterdam), being a resident successively at the nursing homes 'Kalorama' and at 'Joachim and Anna' in Nijmegen.

The next three years, until 1996, he worked as elderly care physician in nursing home Wittenberg in Amsterdam. In 1996 he started to work at VOSON (Vervolgopleiding tot Verpleeghuisarts Nijmegen) and moved to Venlo, to work as elderly care physician at De Professor Dubois Stichting at the same time.

In 1998 he accepted a job as medical manager in nursing home Martinushof, part of De Professor Dubois Stichting.

In 2001 he moved to Sittard to work as elderly care physician in nursing home Schuttershof (Cicero care organization) in Brunssum. In addition, in 2004 he commenced a study at Cardiff University, to achieve a Master in Wound Healing and Tissue Repair (2008).

In 2006 he went back to his former employer in Venlo, after a merger of institutions now called De Zorggroep.

Employed at and supported by De Zorggroep, he started in 2009 an outpatient wound clinic in Venray. In 2010 he started his PhD trajectory 'Prevalence and assessment of (infected) chronic wounds' at Maastricht University, under supervision of Prof. Dr. Jos Schols, Dr. Ruud Halfens and Dr. Ellen Stobberingh.

At the moment the author is still working in the outpatient wound clinic. This wound clinic is currently expanding to additional locations in the south of the province of Limburg.

List of publications

List of publications and presentations

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Award

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Prevalence and assessment of (infected) chronic wounds

Armand Rondas